"I would have everie man write what he knowes and no more."—MONTAIGNE

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EDITORIAL

THE history of intubation over the last forty years is typical of the way the public react to innovations. In 1911 Sir William Milligan brought from Germany a Kuhn's tube. It transformed an ordinary Caldwell Luc operation from a bloody and often a disagreeable occasion, owing to the mutual recriminations of surgeon and anaesthetist as to who was responsible for the unsatisfactory state of affairs, to a period of peace, so serene as to seem unnatural in the atmosphere of an operating theatre of the time.

It was soon seen that the open airway thus obtained was a great help in getting muscular relaxation in abdominal sections. Adverse criticism from those who had not used the new-fangled gadget was widespread and prevented its extended use. The point of the criticism was the blindness of the method, not of course that of the critics. Then came an extension of the use of the laryngoscope by the anaesthetist, and soon after much criticism of the oral route, and so with the advent of Magill's tube a reversion to the blind method, this time through the nose. So fascinated were anaesthetists with the new toy that a visit to the anaesthetic room would provide the visitor with the spectacle of an indiarubber tube jumping up and down much like the float agitated by the movements of a distracted fish. Now apparently the blind method though retained for exceptional cases is falling into disrepute. "Many anaesthetists," says Dr. Franks, "consider that blind intubation is now no longer necessary or desirable, but, as Dr. Nosworthy points out, 'Every now and then, however, the blind method provides the answer to an awkward situation', for this reason it would be a loss if the method fell into complete disuse." So the public (anaesthetist) have described not full circle but five hundred and forty degrees.

THE portrait of Sir Frederic Hewitt which appears on the front cover of this issue was obtained, like the others, with the generous help of our many friends and colleagues, and copied by Miss Barbara Duckworth, artist to the Department of Surgery of the University of Liverpool. To all who have helped us in this matter we wish to express our gratitude. The greatest difficulty was in obtaining a specimen of Hewitt's signature. This difficulty must have been largely due to our own oversight, for it was not until we had approached several possible sources that we thought of Hewitt's own hospital. Through the good offices of Dr. Challis and Mr. Wilding of the London Hospital we were able to obtain what must be one of the few extant originals of the signature, and their co-operation has enabled us to keep the portrait of this great pioneer in line with the others whose worthy successor he undoubtedly was.

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THE MODE OF ACTION OF QUATERNARY AMMONIUM TYPE NEUROMUSCULAR BLOCKING AGENTS

BY

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THE recent finding (Zaimis, Churchill-Davidson and Richardson, 1952; Phillipot and Dallemagne, 1952) that the neuromuscular block produced by decamethonium, a depolarizing agent, is similar in certain mammals to the neuromuscular blocking caused by d-tubocurarine, indicates the necessity for a reconsideration of the mode of action and classification of the quaternary ammonium (R_4N) type neuromuscular blocking agents.

Paton and Zaimis (1952) and Paton (1953) distinguished between three types of neuromuscular block: (1) competitive block; (2) depolarization block; (3) mixed or intermediate block. According to these investigators certain R_4N type neuromuscular blocking agents, e.g. d-tubocurarine, compete with acetylcholine for the cholinergic receptors of the endplate, prevent the access of acetylcholine to these structures and inhibit neuromuscular transmission by interfering with the physiological acetylcholine depolarization of the endplate. They termed the block caused by these compounds competitive neuromuscular blocking. Another group of compounds, e.g. decamethonium, produces neuromuscular blocking by causing prolonged depolarization of the endplate. This depolarization is capable of spreading to parts of the muscle fibre adjacent to the endplate (Burns and Paton, 1951). The block produced by this mechanism was termed depolarization block. Earlier Paton and Zaimis (1949) considered the possibility that the depolarizing agents might act at a site different from that at which d-tubocurarine exerts its effect and Zaimis (1951) suggested that perhaps in certain mammalian species depolarizing neuromuscular blocking agents " might at first adhere in a specific way necessary to produce depolarization at the endplate, their grip eventually changes, with the result that from depolarizing substances they become competitive inhibitors." A third group of compounds, according to Paton (1951), might have partially depolarizing, partially " acetylcholine competing," activity. Such compounds should produce a mixed or intermediate block (Paton and Zaimis, 1952; Paton, 1953).

It hardly seems justifiable to contrast the competitive action of d-tubocurarine and similar compounds with the depolari-

zing action of decamethonium and its congeners. The depolarizing agents, as pointed out by Paton (1953) himself, chemically resemble acetylcholine more closely than the "competitive" neuromuscular blocking agents. Furthermore, under suitable experimental conditions acetylcholine exerts an inhibitory effect at the neuromuscular junction (Burns and Paton, 1951). The depolarizing neuromuscular blocking agents can both block (Paton and Zaimis, 1949), and simulate the excitatory actions of acetylcholine at the endplate (Paton and Zaimis, 1949; Ginzel, Klupp and Werner, 1951); and inhibitors of acetylcholine esterase that cause acetylcholine accumulation at the neuromuscular junction can intensify both the stimulating (Ginzel et al., 1951; Zaimis, 1951) and the blocking activity (Paton, 1951; Bovet-Nitti, 1949; Castello and de Beer, 1950) of depolarizing agents. It therefore seems logical to assume a common site of action for acetylcholine and the depolarizing type neuromuscular blocking agents (Jarcho, Eyzaguirre, Talbot and Lilienthal, 1950; Collier, 1951). A further argument against the classification suggested by Paton and Zaimis is that, in some mammals, decamethonium can cause a neuromuscular block similar to that produced by the competitive agents (Zaimis et al., 1952; Phillipot and Dallemagne, 1952) and that in the rat the neuromuscular blocking activity of d-tubocurarine and decamethonium can be additive (Jarcho, Berman, Eyzaguirre and Lilienthal, 1951).

In the following, a working hypothesis will be presented that endeavours to explain the qualitative (depolarization or anti-depolarization) and quantitative (potency variation) differences in the actions of the R_4N type neuromuscular blocking agents by variations in the chemical structure of these agents and by differences in the properties of the receptor proteins.

Based on the proposed hypothesis, the R_4N type neuromuscular blocking agents can be divided into two, instead of three groups: (1) anti-depolarizing agents—corresponding to the "competitive" agents in the classification of Paton and Zaimis, and exemplified by d-tubocurarine; and (2) depolarizing agents—e.g decamethonium. The members of the first group, under physiological circumstances, have a uniform action at the neuromuscular junction of all amphibian, avian, and mammalian species investigated. These compounds inhibit neuromuscular transmission by preventing the access of acetylcholine to the cholinergic receptors of the endplate (Dale, Feldberg and Vogt, 1936; Cowan, 1936) and thereby decrease or completely abolish the endplate potential. The anti-depolarizing agents show comparatively little species variation in mammals (table I) and without previous excitatory phenomena cause flaccid paralysis. Their effect is counteracted by

TABLE I

*The mg./kg. paralysing doses of d-tubocurarine and decamethonium in various species.**

	Cat	Man	Baboon	Rabbit	Monkey	Mouse	Rat	Frog
Decamethonium	0.03	0.05	0.14	0.15	0.25	0.70	2.5	11.0
d-Tubocurarine	0.3	0.25	—	0.20	0.09	0.12	0.08	5.5

* Paton and Zaimis (1949).

cholinesterase inhibitors (Paton, 1951; Aeschlimann and Reinert, 1931; Briscoe, 1936) and phenolic quaternary ammonium salts (Cowan, 1938; Randall, 1950). These agents also prevent the activity of acetylcholine administered by "close intra-arterial injection."

The behaviour of the depolarizing neuromuscular blocking agents, represented by decamethonium in the ensuing discussion, is not so uniform. Instead of flaccid paralysis they cause contractures in amphibians (Paton and Zaimis, 1949) or avians (Buttle and Zaimis, 1949). Mammals exhibit a marked variation in their sensitivity towards decamethonium (table I). In some mammals (e.g. cat, man) the administration of relatively small mg./kg. doses causes flaccid paralysis preceded by signs of stimulation (Paton and Zaimis, 1949); in other mammals (e.g. monkey) the block produced by larger doses of decamethonium resembles the neuromuscular block caused by the anti-depolarizing agents (Zaimis et al., 1952).

The variation in the response of the neuromuscular junction of different species to the same agent might be explained conveniently by assuming various degrees of resistance towards depolarization by the endplate of different species. It was suggested by Nachmansohn (1952) that the adsorption of acetylcholine changes the configuration of the receptor proteins of the endplate. This change in configuration alters the permeability of the postjunctional membrane to cations and makes possible the $Na+$ and $K+$ shifts that initiate the endplate potential. According to the hypothesis presented, acetylcholine, the physiological depolarizing agent, is capable of changing the configuration of the receptor proteins of all species. Other agents, classified as depolarizing neuromuscular blocking agents, can only do this with the receptor proteins of some species, the configuration of which can be changed easily, and the anti-depolarizing neuromuscular blocking agents, under physiological circumstances, do not depolarize the endplate of any species so far investigated.

The factors determining the type of neuromuscular block caused by the various R_4N type neuromuscular blocking agents are summarized in table II.

It has been shown experimentally that different muscles of the same species can have different sensitivity towards depolarizing agents (Paton and Zaimis, 1951)

TABLE II

Factors determining the type of neuromuscular block produced by quaternary ammonium compounds

Type of neuromuscular blocking agent	Sensitivity of the receptors towards depolarizing influences	Resulting neuromuscular block
Anti-depolarizing (e.g., d-tubocurarine) uniform activity	Low sensitivity (e.g., monkey)	Anti-depolarization block
	High sensitivity (e.g., cat)	
Depolarizing (e.g., decamethonium) variable activity	Low sensitivity	Anti-depolarization block
	High sensitivity	Depolarization block

and that on prolonged administration of decamethonium transition can occur from depolarization block to anti-depolarization block (Zaimis et al., 1952). This might be explained, on the one hand, by differences in the structure of the receptor proteins in various muscles of the same species, and on the other, by changes in the configuration of the receptor proteins on prolonged contact with decamethonium.

The various changes observed in the action of the R_4N type neuromuscular blocking agents in pathological conditions can also be reconciled with the proposed hypothesis. The increased sensitivity of the neuromuscular junction of chronically denervated muscle to acetylcholine (Frank, Nothmann and Hirsch-Kaufmann, 1922; Dale and Gasser, 1926; Gasser and Dale, 1926) might be due to an increased sensitivity of the receptor protein towards configuration changing influences. This tendency might also explain the fact that even anti-depolarizing agents like d-tubocurarine (Jarcho et al., 1951; McIntyre and King, 1943; McIntyre et al., 1945) and gallamine triethiodide (Bulbring and Depierre, 1949) can have a stimulating action at the neuromuscular junction of chronically denervated muscles.

The sensitivity of the receptor proteins towards depolarizing influences can also decrease in pathological conditions. Thus in myasthenia gravis the neuromuscular block caused by decamethonium has the characteristics of an anti-depolarization block (Zaimis et al., 1952). This finding, together with the well-known increased sensitivity of the myasthenic muscle to d-tubocurarine (Bennett and Cash, 1943), can be explained by the assumption that in this disease the receptor protein undergoes changes that decrease its sensitivity towards depolarizing influences. Zaimis, Churchill-Davidson and Richardson (1952) believe that even acetylcholine might have an anti-depolarizing action in myasthenic muscle.

SUMMARY

It has been suggested that all the R_4N type neuromuscular blocking agents compete with acetylcholine for the cholinergic receptors of the endplate. The character of the neuromuscular block caused by these compounds depends on: (1) the chemical structure of the neuromuscular blocking agent and (2) the properties of the receptor proteins. The anti-depolarizing agents (e.g. d-tubocurarine) will produce, under physiological circumstances, an anti-depolarization block at the neuromuscular junction of all species investigated. The type of neuromuscular block caused by the depolarizing agents (e.g. decamethonium) will depend on the properties of the receptor protein of the species in question. In avians, amphibians, and some mammals (e.g. cat) where the configuration of the receptor proteins can be changed relatively easily, decamethonium causes depolarization block. In other mammals (e.g. monkey) where the receptor proteins are less inclined to configuration changes, decamethonium causes an anti-depolarization block.

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Brit. J. Anaesth. (1954), **26**, 399.

THE CLASSIFICATION OF THE MYONEURAL BLOCKING AGENTS

BY

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THE classification of myoneural blocking agents at present accepted at least in Great Britain, divides these drugs into two groups, viz. those which compete with acetylcholine and prevent its access to the muscle end plate, i.e. the competitive blockers, and those which themselves depolarize the end plate with the result that the normal depolarizer, acetylcholine, is no longer able to exert its physiological function. It is, however, admitted already on all sides that substances exist which are capable of blocking transmission across the myoneural junction, yet cannot be assigned to either of these groups. For the want of a better description drugs of this type are referred to as possessing a 'mixed' action (Paton, 1953). The issue has become further complicated. For in order to explain some of the actions of decamethonium, the prototype of the depolarizing myoneural blockers, it has become necessary to postulate that this agent, while initially exerting its typical action, later exerts its paralysing activity by competing with acetylcholine (Zaimis, 1953). It therefore seems as if the classification of agents of this type into the accepted hard and fast groups is not satisfactory.

CLINICAL CONSIDERATIONS

This difficulty becomes even more apparent when the phenomena associated with the clinical administration of myoneural blocking agents in anaesthesia is considered. In the last few years the author has tested two synthetic 'curarizing' drugs (benzoquinonium and laudexium) which were found on laboratory testing to be 'competitive blockers' like d-tubocurarine. In clinical use, however, neither of these agents produced relaxation with exactly the same characteristics as those of the prototype com-

TABLE I

The clinical properties of relaxant drugs

	Decamethonium	Benzoquinonium	Laudexium	d-Tubocurarine
Useful partial paralysis ...	—	+	+	++
Neostigmine reversibility	—	±	+	++
Tendency to cumulation	++	±	±	—
Type of recovery	Abrupt	Gradual	Gradual	Gradual

petitive blockers (Hunter, 1952, 1954). Two other agents, gallamine triethiodide and dimethyl-tubocurarine, also classified in the laboratory as competitive blockers, on the other hand did seem in clinical use to possess actions at the myoneural junction qualitatively comparable to d-tubocurarine.

A possible way out of this difficulty is suggested by a comparison of the clinical effects of the myoneural blocking agents already referred to (table I). It will be seen that there is no sharp differentiation of the drugs into two distinct groups but a gradual transition in type of action from that of decamethonium with its abrupt recovery of muscle power, its marked sparing of the diaphragm, its tendency to produce cumulative effects and the virtual absence of neostigmine reversibility to the action of the typical competitive blocker like d-tubocurarine. In this group the characteristic features are a gradual disappearance of the paralysis produced by a single dose, negligible diaphragmatic sparing, virtually no tendency to cumulation in ordinary clinical doses and complete reversibility by neostigmine. Benzoquinonium and laudexium occupy intermediate places in this table and have properties to correspond. Clinical experience, therefore, suggests that it is more profitable to regard relaxant drugs not as members of one of two sharply defined groups but as a series of agents all possessing the same basic properties, though in varying degrees.

EXPERIMENTAL EVIDENCE

If the actions of relaxant drugs observed in the laboratory are reviewed it will be found that there is a comparable gradation of effect. This is particularly marked in relation to spontaneous acetylcholine sensitizing power.

Acetylcholine Potentiation.

The various evidences of acetylcholine potentiation produced by some typical myoneural blocking agents will be seen in table II. In their first study of decamethonium, Paton and Zaimis (1949) observed that if this drug was given to a cat whose gastrocnemius was being stimulated by way of the motor nerve, the first effect was an increase in the force of the twitch, which was in fact converted into a short tetanus. Riker and his colleagues (1949) observed the same phenomenon when drugs like Tensilon were beginning to take effect. Winter and Lehmann (1950) who investigated the action of dipropa-

TABLE II

The acetylcholine potentiating actions of the relaxant drugs

	Tensilon	Deca-methonium	Dipro-pamine	Benzo-quinonium	Laud-exium	d-Tubocurarine and gallamine triethiodide
'Convulsions' in mice	+++	++	+	+	+	—
Antagonism to d-tubocurarine...	++	+	+	—	—	—
Augmentor effect on muscle twitch	++	+	±	—	—	—
Action on intra-arterial injection	Con-traction	Con-traction	Paralysis	Paralysis	Paralysis	Paralysis

mine did not find any such changes in the cat but did observe that the drug increased the contraction of a frog's rectus muscle produced by acetylcholine.

There is a close parallelism between these effects of myoneural blocking agents and their powers of producing contraction of a muscle when injected into the artery going directly to it. Decamethonium produces this response (Paton and Zaimis, 1949); so also do drugs like Tensilon (Riker et al., 1949) apparently in greater degree. Dipropamine does not possess this property (Hunter, 1953a) but like the drugs at the other end of the scale, benzoquinonium, laudexium, d-tubocurarine and gallamine triethiodide, it produces paralysis without preliminary stimulation. It is, however, possible with special techniques to obtain evidence that even the last of these agents produces a little stimulation before it paralyses skeletal muscle (Bulbring and Depierre, 1949; Riker and Wescoe, 1951).

The author has observed a similar gradation of effect when these drugs are given to mice. When a large dose of Tensilon is given there can be seen obvious fibrillation, fasciculation and vigorous tonic contractions of the limb muscles. Sometimes, indeed, these are forcible enough to jerk the animal into the air. They are not true convulsions but it is convenient to refer to them by this title. They are also obvious after the administration of decamethonium and like drugs and when dipropamine has been injected in large doses (Hunter, 1953a). They are produced by laudexium and benzoquinonium though in less marked degree, while after d-tubocurarine and gallamine triethiodide, the syndrome of exitus usually consists of head drop and respiratory paralysis with virtually no spontaneous muscular activity.

Another piece of evidence concerning the acetylcholine potentiating action of these agents is found in their power of reversing the paralysis produced by d-tubocurarine and gallamine triethiodide. Tensilon possesses this action in very marked degree. Neither decamethonium nor its di-thia analogue (Ro 3-0386) (Hunter, 1953b) is as potent in this respect but reversal can quite readily be demonstrated, though its action is evanescent. Dipropamine also reverses paralysis produced by d-tubocurarine (Winter and Lehman, 1950), while benzoquinonium and laudexium lack this action completely. Indeed their action after d-tubocurarine is to intensify the myoneural block.

Though gradation in the properties of myoneural blocking agents is most marked in relation to their power of potentiating

TABLE III

Some actions of relaxant drugs in experimental animals

	Tensilon	Deca-methonium	Mytolon	Laudo-lissin	Gallamine triethio-dide	d-Tubo-curarine
Histamine release	—	—	—	+	+	++
Sympathetic ganglion block ...	—	—	—	+	+	+
Parasympathetic ganglion block	—	—	—	—	+	+
Muscarinic action	+	—	—	—	—	—

acetylcholine it can also be seen in other aspects of their action at the muscle end-plate. The author and most other workers in this field have observed that when d-tubocurarine or gallamine triethiodide is given to a cat there is a very marked weakening of the response of a muscle to rapidly repeated stimuli, i.e. to a tetanus. This is by no means so obvious when laudexium and benzoquinonium have been injected and is then apparent only during the deepest phases of the action of decamethonium and like drugs.

Neostigmine Reversibility.

There is a similar gradation in the response of the paralysed animal to neostigmine. The action of d-tubocurarine and gallamine triethiodide are promptly and completely reversed by this drug. In the case of laudexium the antagonism is not so satisfactory in the cat (Hunter, 1955) while the reversal of benzoquinonium by neostigmine has been reported only in the dog and that from comparatively slight degrees of myoneural block (Hoppe, 1950). This varied response to neostigmine is even more marked when the antagonist is used to try to protect mice against lethal doses of the relaxant. With gallamine triethiodide, it affords nearly complete protection against an L.D.95. With laudexium the protection is less marked while neostigmine increases the toxicity of benzoquinonium (Hunter, 1952), though this may be due to the summation of the anticholinesterase activity of these two drugs.

Effects on Autonomic Nervous System.

Gradation of activity can also be seen in the effects of the myoneural blocking agents on the synapses of the autonomic nervous system. Tensilon has a very mild muscarinic action which is probably exerted at the nerve endings of the parasympathetic but it does not block ganglion conduction. Decamethonium and dipropamine have little action on any part of the autonomic nervous system. The effects of benzoquinonium on the parasympathetic are masked by its powerful anticholinesterase action, but it has no action on the transmission through the sympathetic ganglia. Laudexium produces block at this latter site but its activity is only one quarter of that of d-tubocurarine. Gallamine triethiodide is less active than d-tubocurarine as a blocker of sympathetic ganglia in the cat (Randall, 1951) but in man its most obvious action is the interruption of the parasympathetic which it produces.

Gradation of Chemical Structure.

Finally the gradation is not confined to pharmacological activity. It can be seen in the chemical structure at least of the relaxants which the author has tested. In these there can be seen a gradual transition from the simple phenyl-alkyl-ammonium structure of Tensilon to the double ended compounds of high activity like decamethonium, dipropamine and benzoquinonium. A further development is shown in the last of these compounds which is combined with benzyl chloride instead being a simple salt of an inorganic acid. In laudexium the terminal trimethylammonium group is replaced by the complex nitrogen containing ring of isoquinoline. Finally in d-tubocurarine the decamethylene chain is replaced by a series of benzene ring linkages. Gallamine

triethiodide does not fit very clearly into this scheme of things but it is quite atypical in that it contains three quaternary groups which are triethyl ammonium and not the trimethylammonium structures usually associated with myoneural blocking activity.

DISCUSSION

There is nothing in the conception of gradation of activity which conflicts with current pharmacological teaching. It is well recognized that many drugs have an initial stimulatory and a subsequent paralysing effect and this is particularly common in those exerting effects on the cholinergic synapses of the autonomic nervous system. In fact it has long been known that some drugs, e.g. hexamethonium, paralyse the sympathetic without preliminary stimulation, while others like nicotine produce marked initial activity before interrupting the function of these ganglia. It is therefore not surprising that agents acting at the motor end-plate should also have a variable amount of stimulatory activity before they produce acetylcholine block at the site of their action. With this in view, it is suggested that the myoneural blocking agents be regarded not as two distinct groups of substances but as drugs occupying places on a ladder, those at the bottom possessing very marked initial stimulatory effects while those at the other end are almost pure depressors with virtually no initial stimulatory effect.

The substitution of the classification here suggested offers two advantages over that at present in use. From the clinical point of view it will put an end to the misleading description of new myoneural blocking agents. It will no longer be found that agents which have been described in the laboratory as 'competitive blockers' in fact prove to possess only some of the properties of d-tubocurarine and in consequence are less useful clinically. Secondly, by placing the emphasis on the amount of acetylcholine potentiation exerted by drugs of this type, rather than on their physiological effect at the end-plate it may be possible to obtain a reconciliation of many of the contradictory results obtained by workers studying myoneural blocking agents in the laboratory.

SUMMARY

The existing classification of myoneural blocking agents is misleading especially when applied to their clinical use. It is suggested that instead of describing drugs of this type as belonging to two hard and fast groups they should be regarded as substances possessing essentially the same properties but those in varying degree. They differ mainly in the amount of overactivity which they produce at the myoneural junction before paralysis develops. If they are graded on this basis it would appear that many of their other properties, such as neostigmine reversibility, their action on the effect on a tetanus and perhaps even their ganglion blocking activity will show a more or less comparable variation.

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BOOK REVIEW

Fluid Balance in Surgical Practice. By L. P. Le Quesne. Published by Lloyd Luke Ltd., July 1954. Pp. 130; 40 illustrations. Price 17*s.* 6*d.*

Of recent years great interest has been taken in the distribution of fluid and electrolytes in the human body, and seeing the body is made up of no less than 70 per cent of H_2O it is obvious that a knowledge of its distribution and functions is a matter of the utmost importance. Until we know the normal we are not in a position to appreciate modification thereof, such for example as takes place when the body is subjected to surgical interference

These changes are described. They consist of water and salt retention in the first 24 to 48 hours following operation, and are attributed in the main to the secretion of the posterior pituitary anti-diuretic hormone. Many patients have lost their lives following surgical interference, not because of any lack of surgical dexterity but simply on account of being inadequately prepared for operation. The author points out that post-operative morbidity and mortality are significantly higher in patients in whom the distribution of H_2O and electrolytes is abnormal; also he stresses that the abnormality is less easily corrected after operation than before. A pre-operative assessment in all doubtful cases is therefore essential and consists of a careful clinical appraisement of the patient's condition. This should take note of the following points:

(1) Mental condition.
(2) Blood pressure.
(3) Condition of skin, subcutaneous tissue, mouth and muscle tone.
(4) Urine—quantity, specific gravity and chloride concentration.
(5) Blood urea.

If there is any deficiency of salt or H_2O this must be remedied by the mouth if possible, as this is a safer route than by the veins. This sounds simple, but in point of fact the interpretation of the results of examination, and the various tests applied, requires both skill and experience, and the cases illustrated in Appendix B provide a most useful guide.

Alike to the student, the practising surgeon and the anaesthetist, to whom this is a matter of great importance, this book will prove an up-to-date account of a subject of great interest.*

E. Falkner Hill

*The author points out there is a mistake in the figures on p. 87. For the two solutions described read:

1. KCl 3.0 gm./L (K 40 m.equiv./L: Cl 40 m.equiv./L)
2. KCl 3.0 gm./L: Na Cl 2.25 gm./L (K 40 m.equiv./L Na 40 m.equiv./L: Cl 80 m.equiv./L)

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NISENTIL (1, 3, DIMETHYL-4-PHENYL-4 PROPIONOXY PIPERIDINE): A NEW SUPPLEMENT FOR NITROUS OXIDE-OXYGEN, THIOPENTONE (PENTOTHAL SODIUM) ANAESTHESIA

BY

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THE pharmacological approach to general anaesthesia should be based upon the selective activity and controllability of the agents used. Such a method will allow the anaesthetist to avoid unnecessary depression of vital mechanisms and will enable him to regulate the duration and degree of anaesthesia to suit the needs of the operation. For muscular relaxation, this degree of controllability has already been met by the use of suxamethonium in continuous intravenous drip (Foldes, Machaj, Hunt and McNall, 1952; Foldes, McNall and Borrego-Hinojosa, 1952). The idea of combining various anaesthetic agents was first suggested by Crile and Lower (1914) and Lundy (1926). In recent years, various analgesic agents have been used in repeated small intravenous doses to supplement nitrous oxide-oxygen, thiopentone anaesthesia (Neff, Mayer and de la Luz Peralez, 1947; Brotman and Cullen, 1949). By using these analgesic supplements satisfactory depth of anaesthesia can be provided by smaller quantities of thiopentone, resulting in earlier postoperative recovery. Pethidine (meperidine) has been used most widely for this purpose (Mushin and Rendell-Baker, 1949; Brotman, Cullen and Wilkins, 1950; Cullen, 1950; Neff, Mayer and Thompson, 1950).

Nisentil, 1, 3, dimethyl-4-phenyl-4 propionoxy piperidine, was first synthesized by Lee in 1947 (Ziering and Lee, 1947) and is structurally similar to pethidine (see figure 1).

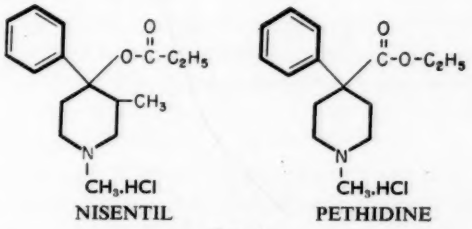

FIG. 1

In both human (Gross, Holland and Schueler, 1948) and animal (Holland and Gross, 1948) experiments no development of tolerance could be observed with Nisentil. Vomiting, nausea, pruritus and other side effects were less frequently encountered with Nisentil than with methor-

phinan or morphine (Lee and Hasegawa, 1950; Lee and Pfeiffer, 1951). Nisentil, like other analgesics, produces a hyperglycaemia which parallels its analgesic action in duration (Kimura and DeBoer, 1951; Kimura, DeBoer, Walts and Keith, 1951; DeBoer, Keith and Walts, 1952; Kimura, Keith and Foster, 1952). The effects of an intravenously administered therapeutic dose last about 45 minutes (Floody, 1954). The mechanism by which Nisentil is decomposed has not yet been clarified; it has been assumed that the liver plays an important role in this process.

So far, Nisentil has been primarily used for the production of analgesia in the first stage of labour (Hapke and Barnes, 1949; Smith and Nagyfy, 1949; Thelen, 1949; La Forge, 1951; Lund, 1951; Pfeiffer, 1951; Kane, 1953). For this purpose, Nisentil was administered subcutaneously in 40–60 mg. doses to a total of over 2,000 cases. Satisfactory analgesia was obtained in 80–95 per cent of the parturients. Drowsiness and sedation were noted, but the patients were easily roused and mentally clear. Dizziness was the most frequently observed side effect.

MATERIAL AND METHODS

In the present study, Nisentil was used for the supplementation of nitrous oxide-oxygen, thiopentone anaesthesia in 756 patients. In a control group of 600 patients pethidine was used as the supplementing agent. Both groups were further subdivided as follows: (1) patients who received no muscle relaxant; (2) patients who received relaxant for intubation only; (3) patients who received relaxants throughout anaesthesia (table I).

TABLE I

Classification of cases with reference to the type of analgesic and the use of muscle relaxant

	Number of cases with	
	Pethidine	Nisentil
No muscle relaxant used	200	290
Relaxant for intubation	200	145
Relaxant for maintenance	200	321
Total	600	756

The age and sex distribution of both groups is shown in table II and the types of operations for the three subdivisions of both groups are shown in table III.

Anaesthetic Management.

After the patient's mouth and pharynx had been sprayed with a topical anaesthetic agent enough thiopentone was administered to permit the insertion of an oropharyngeal airway. Nitrous oxide-oxygen was then administered by the method of Foldes, Ceravolo and Carpenter (1952) and the first dose of Nisentil was given. The initial dose varied with the age, weight, physical condition and habits of the patient; the average was 7.5 mg. In

TABLE II

Decade of life	Number of patients with Pethidine	Nisentil
Age distribution		
10–20	32	63
21–30	105	119
31–40	167	175
41–50	135	201
51–60	111	113
61–70	35	50
71–80	15	35
Total	600	756
Sex distribution		
Male	197	320
Female	403	436
Total	600	756

TABLE III
Types of operations

	Number of cases with Pethidine	Nisentil
NO MUSCLE RELAXANT USED		
Skin graft, biopsy, ganglionectomies	35	58
Herniorrhaphy	19	28
Various orthopaedic procedures	23	26
Vein ligation and stripping	27	44
Excision breast cyst, simple and radical mastectomy	14	30
Perineorrhaphy	16	17
D. & C. cervical biopsy or coninization	48	62
Cystoscopy, circumcision	18	25
Total	200	290
RELAXANT FOR INTUBATION		
Thyroidectomy	39	34
Mastoidectomy and fenestration	24	18
Lumbar sympathectomy, laminectomy, spinal fusion	33	22
Tonsillectomy	23	14
Coccygectomy, pilonidal cystectomy	14	15
Radical neck dissection and other neck surgery	25	22
Various ophthalmologic procedures	23	13
Plastic procedures of the face	19	7
Total	200	145
RELAXANT FOR MAINTENANCE		
Hysterectomy, various intraperitoneal gynaecologic procedures	37	51
Gastric surgery	22	35
Appendicectomy	24	45
Gall bladder surgery	53	78
Ventral or incisional herniorrhaphy	24	29
Large bowel surgery	21	49
Various genito-urinary procedures	14	24
Miscellaneous abdominal procedures	5	10
Total	200	321

old, weak, debilitated or heavily premedicated individuals and in patients with liver disease or hypothyroidism, the initial dose was decreased to 3.5 mg. Conversely, in large robust subjects, an initial dose of 12 to 15 mg. was used. The size of subsequent fractional doses varied according to the effects of the initial dose. Apart from the usual signs of lightening anaesthesia, an increase in the respiratory rate to over 20 per minute was considered an indication for the administration of a supplementary dose. The average interval between doses was 8 to 20 minutes. Occasionally, fractional doses had to be given more frequently early in the anaesthesia to obtain the desired depth. As the anaesthesia progressed fractional doses were required less frequently. After induction, no further thiopentone was given unless adequate anaesthesia, characterized by insensitivity to reflex stimulation originating in the operative area, could not be obtained without undue depression of the respiratory rate. In patients where muscle relaxants were used the first dose of Nisentil was administered, and its effects noted, before the relaxant was given.

Method of Evaluation.

Two criteria have been used in comparing the relative efficiency of Nisentil and pethidine for the supplementation of nitrous oxide-oxygen, thiopentone anaesthesia: (1) the mg./minute thiopentone dose used in operations of various durations; (2) the percentage of patients reacting to auditory and tactile stimulation within five minutes of the conclusion of surgery.

RESULTS

It is evident from table IV that the mg./minute doses of thiopentone diminished progressively with increasing duration of anaesthesia. It will also be seen from this table that the mg./minute thiopentone requirements with Nisentil were significantly smaller than with pethidine. Pethidine is a longer-acting analgesic and is therefore more cumulative

TABLE IV

The mg./minute thiopentone requirements with Nisentil and pethidine supplementation

Duration of anaesthesia	No muscle relaxant		Relaxant for intubation		Relaxant for maintenance	
	Pethidine	Nisentil	Pethidine	Nisentil	Pethidine	Nisentil
0–30	39.4 ± 4.5*	17.3 ± 1.6	—	—	—	—
30–45	24.2 ± 1.6	13.4 ± 0.8	—	—	—	—
45–60	19.2 ± 0.9	9.8 ± 0.8	†21.4 ± 1.5	†14.4 ± 1.2	†18.8 ± 0.7	†12.4 ± 0.9
60–90	16.7 ± 0.8	7.7 ± 0.7	17.0 ± 0.8	8.4 ± 0.4	14.5 ± 0.7	8.0 ± 0.2
90–120	12.5 ± 0.5	5.9 ± 0.4	13.2 ± 0.4	6.1 ± 0.4	11.9 ± 0.4	6.4 ± 0.7
120–150	10.5 ± 0.5	4.5 ± 0.4	10.9 ± 0.5	4.9 ± 0.7	10.2 ± 0.4	5.2 ± 0.4
150–180	——	—	9.7 ± 0.5	4.1 ± 0.2	9.6 ± 0.4	4.2 ± 0.8
180 and over	——	—	—	—	8.2 ± 0.3	3.2 ± 0.3

* Standard error. † Includes all cases up to one hour.

than Nisentil. The mg./minute doses of Nisentil and pethidine also diminished with increasing length of anaesthesia; this decrease, however, was more marked with pethidine than with Nisentil (table V). As would be expected, with the smaller quantities of thiopentone used, a greater percentage of patients reacted to stimulation at the termination of surgery in the Nisentil group than in the pethidine group (table VI).

It has been our impression that Nisentil had a greater effect on respiratory rate than depth. In contradistinction, pethidine seemed to have a more pronounced effect on the tidal volume than on the respiratory rate. Neither Nisentil nor pethidine had any consistent effect on pulse rate or blood pressure.

DISCUSSION

The analgesic agent used to supplement nitrous oxide-oxygen, thiopentone anaesthesia should be short-acting, have minimal cumulative effect and therefore be readily controllable. We have found that Nisentil, employed as described above, closely approaches these requirements. Using small doses of this agent it was possible to maintain satisfactory depths of general anaesthesia during surgery with less thiopentone than would otherwise have been used. Furthermore, the use of repeated small doses of Nisentil did not result in undue depression of respiration or other vital functions. In a few cases not included in this study Nisentil was used in larger doses to decrease further the thiopentone requirements. Marked slowing of

TABLE V

The mg./minute dose of Nisentil and pethidine used for the supplementation of N_2O—O_2 thiopentone anaesthesia.

Duration of anaesthesia	No muscle relaxant		Relaxant for intubation		Relaxant for maintenance	
	Pethidine	Nisentil	Pethidine	Nisentil	Pethidine	Nisentil
0–30	1.39 ± 0.13*	0.60 ± 0.08	—	—	—	—
30–45	0.98 ± 0.12	0.57 ± 0.02	—	—	—	—
45–60	0.72 ± 0.08	0.49 ± 0.02	†0.87 ± 0.03	†0.53 ± 0.03	†0.75 ± 0.03	†0.53 ± 0.02
60–90	0.65 ± 0.07	0.44 ± 0.03	0.60 ± 0.02	0.48 ± 0.02	0.61 ± 0.02	0.43 ± 0.02
90–120	0.58 ± 0.08	0.35 ± 0.01	0.52 ± 0.02	0.45 ± 0.03	0.54 ± 0.03	0.41 ± 0.01
120–150	0.43 ± 0.03	0.29 ± 0.01	0.48 ± 0.02	0.39 ± 0.01	0.48 ± 0.02	0.37 ± 0.02
150–180	—	—	0.43 ± 0.02	0.35 ± 0.02	0.46 ± 0.02	0.33 ± 0.02
180 and over	—	—	—	—	0.38 ± 0.02	0.28 ± 0.01

* Standard error. † Includes all cases up to one hour.

TABLE VI

The percentage of patients reacting after surgery

Duration of anaesthesia	No muscle relaxant		Relaxant for intubation		Relaxant for maintenance	
	Pethidine	Nisentil	Pethidine	Nisentil	Pethidine	Nisentil
0–30	36	62	—	—	—	—
30–45	48	67	—	—	—	—
45–60	51	77	48*	72*	44*	70*
60–90	60	84	55	87	56	81
90–120	61	87	62	90	62	84
120–150	64	88	66	91	64	85
150–180	—	—	65	91	66	88
180 and over	—	—	—	—	66	89

* Includes all cases up to one hour.

the respiratory rate, necessitating assisted respiration, was encountered in almost every case and, in contrast to our expectations, post-operative recovery was delayed rather than expedited.

A similar investigation with Nisentil was carried out independently by one of us in England; the results of this unpublished work correspond closely with our findings (Swerdlow, 1954).

SUMMARY

(1) The use of small intravenous doses of Nisentil has been described for the supplementation of nitrous oxide-oxygen, thiopentone anaesthesia.

(2) The mg./minute dose of thiopentone required for operative procedures of various duration and the percentage of patients reacting to stimulation at the termination of surgery were compared in two series receiving Nisentil and pethidine respectively.

(3) The mg./minute dose of thiopentone was significantly lower with Nisentil than with pethidine supplementation.

(4) The percentage of patients reacting to stimulation at the termination of surgery was greater in the Nisentil than in the pethidine group.

(5) The use of Nisentil as a supplementary agent permitted increased controllability of the depth of anaesthesia without undue depression of respiration and other vital functions.

(6) The use of large doses of Nisentil resulted in respiratory depression and decreased controllability.

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WORLD CONGRESS OF ANAESTHESIOLOGISTS

The World Congress of Anaesthesiologists will be held at Scheveningen near The Hague (Holland) from September 5 to September 10, 1955. The following will be the main subjects for discussion:

(*a*) Relaxants, Ganglion blockers
(*b*) Hypotension, Phenothiazine
(*c*) Hypothermia, Hibernation
} Pharmacological, physiological and clinical aspects.

(*d*) Respiration, Circulation.
(*e*) Teaching of Anaesthesia.
(*f*) Free subjects.

It is the intention that the Official Foundation of the World Federation of Societies of Anaesthesiologists should take place in the course of this Congress. For the entertainment of the participators' ladies a programme has been drafted and a ladies committee will be formed to receive them. A Preliminary Programme will be distributed in the course of this year.

The Congress fee will be 35 Dutch Guilders. It will be reduced to 25 Dutch Guilders for those who send in their application form before March 31, 1955.

All correspondence should be addressed to the Executive Manager, World Congress of Anaesthesiologists, Bilthoven, Holland.

Brit. J. Anaesth. (1954), **26**, 411.

ANAESTHESIA FOR TONSILLECTOMY*

BY

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THIS paper is a short account of the several anaesthetic techniques used in over 1,000 cases of tonsillectomy at Glasgow Ear, Nose and Throat Hospital during 1948–1953. The subject falls naturally into two parts:

I. Anaesthesia for the removal of tonsils and adenoids in children (860 cases); and

II. Anaesthesia for dissection of tonsils in adults (151 cases).

In each case the anaesthetic technique varies with the operative requirements, themselves a variable factor, especially in the child.

IN CHILDREN

Operative Requirements.

In the cases of this series, tonsillectomy in children was carried out by one of three methods, the main difference between them from the anaesthetist's point of view being one of duration, thus:

(1) The Sluder-Ballenger guillotine.

(2) The Layton tonsil enucleator (screw guillotine).

(3) The dissector and snare.

Divergent views (not unrelated to the anaesthesia) are expressed by throat surgeons as to the respective merits of these procedures. Thus McLaggan (1937) states: "Dissection gives uniformly better results, principally because it requires the administration of an anaesthetic which is prolonged until the operation is completed to the satisfaction of the surgeon." He describes guillotine enucleation under ethyl chloride as "a hit or miss procedure," and goes on to say: "even in the hands of expert operators and anaesthetists there is a percentage of incomplete operations, usually due to anaesthetic difficulties. This percentage rarely falls below 10 and is entirely unjustifiable. . . . The greatest objection to the guillotine method is lost when a prolonged ether anaesthetic is given." On the other hand, this sweeping condemnation of the use of the guillotine is countered by Turner (1952) who described its use in children anaesthetized with 3–5 ml. of ethyl chloride from a Guy's inhaler.

In the present series, 819 children were anaesthetized for removal of tonsils and adenoids. In over 90 per cent of cases the guillotine or enucleator was used and ethyl chloride was the main anaesthetic agent. Only 2 cases returned for removal of tonsil tags. One could not be dogmatic about this figure, however, since the cases were not normally seen later than two weeks post-operatively.

Even in the small number of cases where the dissector and snare were used the surgeon was usually able to complete his work satisfactorily within the short period

* Read to the Glasgow and West of Scotland Society of Anaesthetists on January 22, 1954.

of anaesthesia provided by a single dose of ethyl chloride in the average child of 5–6 years. In 73 cases, however, where it was anticipated that rather more anaesthetic would be necessary, usually in bigger children (up to 14 years) supplementary ether was added.

Although the operation is of such short duration, deep anaesthesia with good muscular relaxation is essential to success for three reasons: (1) The masseters (powerful muscles, even in the child), the medial pterygoids (which work at a great mechanical advantage) and the temporales muscles must be well relaxed to allow easy atraumatic insertion of the gag (preferably Jenning's). (2) The palato-glossus m. (in the ant. pillar), the palato-pharyngeus m. (in the post. pillar of the fauces) and sup. constrictor m. of the pharynx (which lies deep to the tonsillar bed) must all be relaxed to allow the entire tonsil to be easily squeezed into the ring of the guillotine. (3) The pharyngeal reflex must, of course, be abolished.

The final and probably the most important requisite is an immediate return of the cough reflex on completion of the tonsillectomy and before adenoidectomy is begun. If the patient is too deep at this stage, the surgeon should wait (having placed a swab in each tonsil bed) until the anaesthesia lightens sufficiently before removing the adenoids.

Thirty-nine cases of adenoidectomy alone are included in the present series, for the anaesthetic technique is similar, although less exacting. All that is required here is sufficient relaxation of the jaw for the insertion of the gag, as the operation is over in a few seconds. At the same time, palatal and pharyngeal movement should not be too vigorous while the curette is being used, lest damage occur to Passavant's bar—that part of the superior constrictor which forms a sphincter with the soft palate. In most cases, the St. Clair Thomson curette was used, but the La Force Adenotome was preferred in some. Trivial as this operation may be, Thomson and Negus (1937) reported that "No inconsiderable number of deaths during this operation have been recorded, and almost every one attributable to the anaesthetic." There were no deaths in this series.

Anaesthetic Technique.

The question of premedication for these children has received much attention. Atropine gr. 1/100 (0.65 mg.) is, of course, essential, not only to prevent the copious secretion of mucus by the child, but in order to protect against primary cardiac failure due to vagal stimulation.

Opinions differ as to the advisability of giving a sedative in addition—bearing in mind its possible effect on the vital cough reflex. Pentobarbitone or phenobarbitone by mouth has been prescribed, while rectal paraldehyde has been suggested to avoid "psychic trauma."

Thus Thomson and Negus (1948) advise pentobarbitone gr. $\frac{1}{2}$ per stone (5 mg./kg.) of body weight by mouth, and paraldehyde dr. 1 per stone (0.6 ml./kg.) of body weight per rectum; yet there is a statement in the same paragraph that "the operation is usually performed in the morning so as to give time for recovery before nightfall"! In a previous edition however (Thomson and Negus, 1937) the same authors advised against sedation or basal narcosis. Methylpentynol may prove

of some value in this respect (Rendell, 1954).

The cases in the present series received atropine only. A skilful nitrous oxide induction, using the hands in place of a face mask (Tindal, 1948) and coupled with the use of suggestion, carries less risk of producing psychic trauma in a child than the administration of any drug per rectum.

Anaesthesia is induced with nitrous oxide, which is then turned off and 3–6 ml. of ethyl chloride with oxygen administered in the familiar Y-piece attachment to the Boyle's machine.

Almost every child can be *coaxed* to sleep with nitrous oxide (Pinkerton, 1948).

724 cases were anaesthetized in this way (tables I and II).

TABLE I
Anaesthesia for tonsillectomy

	No. of cases
IN CHILDREN	
Tonsillectomy and adenoidectomy	819
Adenoidectomy only	39
Removal of tonsil tag	2
	860
IN ADULTS	
Tonsillectomy (Dissection)	151
Total number of cases	1011

DISCUSSION

It has been said, presumably because of its potency, that the safest way to administer ethyl chloride is on an open mask.

The method described is preferable for the following reasons:

(1) Nitrous oxide is a safer agent with which to induce anaesthesia than is ethyl chloride.

(2) Re-breathing of CO_2 in the closed system makes for a quicker and therefore safer induction.

(3) A small and accurate dosage is possible only by this method—or by some form of vaporizer, such as that described by Bromage (1950); it is thus practically impossible to administer an overdose.

(4) The high oxygen atmosphere counteracts any tendency to laryngeal spasm.

But ethyl chloride, however administered, has a high Coefficient of Partition and is not without effect on the cardiovascular system: there is some direct depression of the myocardium and increased irritability of the conducting mechanism; the cardiac output may be decreased and the blood pressure fall steeply. While these effects result in very satisfactory operating conditions, they can hardly be said to be altogether laudable,

TABLE II
Anaesthetics used for tonsillectomy
Nitrous oxide and oxygen in each case plus:

Anaesthetic agent	In children		In adults	
	No.	%	No.	%
Ethyl chloride	724	92.6		
Ethyl chloride and ether	73			
Vinyl ether	49	5.8		
Ethyl ether	14	1.6	49	57.6
Trichlorethylene and ether			38	
Chloroform			17	11.2
Thiopentone, suxamethonium and trichlorethylene ...			47	31.2
Totals	860	—	151	—

otherwise chloroform would be the anaesthetic of choice for this operation!

In looking for a drug with the acknowledged safety of ethyl ether but with a greater speed of induction and excretion, vinyl ether seemed the obvious choice. Forty-nine cases were anaesthetized with this drug using 3–6 ml. by exactly the same technique as that described for ethyl chloride. Induction was effected even more rapidly, but the duration of anaesthesia achieved was correspondingly shorter, not as a rule exceeding 30 seconds. It was, therefore, suitable for use only with the guillotine. Relaxation was good, while there was generally a little more bleeding which was easily controlled by suction.

Thus nitrous oxide-oxygen-vinyl ether-ethyl ether would appear to be a very safe anaesthetic sequence for this operation, providing good relaxation for 2–3 minutes.

Ethyl ether itself was used in 14 cases where an even longer anaesthetic was required. With this drug anaesthesia of 5 minutes duration could easily be achieved by the single dose technique. Accurate timing of the premedication is essential.

If the child's nasal airway is poor, a small oro-pharyngeal airway should be inserted as soon as possible.

Immediate Post-Operative Period.

As soon as the naso-pharynx is cleared of adenoids the child is turned on to his left side and the face douched with cold water. Close observation during the immediate post-operative period is an integral part of the operation, not only to ensure that he has fully recovered his cough reflex but also (and some surgeons stress this) to see that bleeding is minimal. The use of the sucker during operation is, of course, literally a vital procedure. The lateral position is maintained during transit to ward and bed. Post-operative sedation is limited to ac. acetylsalicyl, gr. 5 (320 mg.) crushed in a little orange juice, or Nepenthe, 1 minim (0.06 ml.) per year, similarly administered.

IN ADULTS

Dissection of tonsils in the adult may be carried out under local or general anaesthesia.

Local Anaesthesia.

In the present series of cases this technique has not been employed on account of the following disadvantages (Hewer, 1953):

(1) "There now seems small reason for subjecting patients to a technique which at best can only be described as unpleasant."

(2) It is unsuitable for fibrotic tonsils.

(3) There is an increased risk of sepsis; in one series of deep cervical infections following tonsillectomy over 90 per cent of cases were found to have had local anaesthesia.

(4) Pulmonary complications are also commoner following local anaesthesia.

General Anaesthesia: Operative Requirements.

Dissection of tonsils including the use of the Boyle-Davis gag is almost the universal practice in the adult. This requires 20–30 minutes anaesthesia by the nasal endotracheal route. The practice of insufflating the anaesthetic gases down the side tube of the gag has little to commend it.

The passage of an endotracheal tube through the nose, however, carries with it certain risks:

(1) *Infection* may be carried from the pharynx to the lungs (Dawkins, 1937), or to the nose on extubation, causing adhesions (Dingley, 1943).

(2) *Trauma* to the nose, pharynx or larynx may occur even with gentle handling and in the absence of bleeding. Wylie (1950), discussing the hazards of intubation, shows a high incidence of sore throat after intubation in 100 cases—not throat cases (see table III).

TABLE III (WYLIE, 1950)
Incidence of sore throat after intubation
(not throat cases)

	Sore throat		
No. of cases	Absent	Mild	Severe
100	30	57	13

Gillies (1953) states that pain originating in the pharynx or trachea following intubation can be avoided by the use of a hygroscopic lubricant such as glycerine on the tube. He also recommends (Gillies, 1951) the use of polyvinyl tubes which soften at body temperature and thus prevent pressure being exerted, for example, by the tip of the tube on the tracheal wall.

Adenoids, too, form a definite hazard during nasal intubation. On this subject Magill (1952) states: "The use of the nasal route (for intubation) in the dissection of tonsils is clearly inadvisable where adenoids are present," and mentions that an oro-tracheal tube may be incorporated in the tongue piece of the Davis gag by a special metal device.

Further, damage may occur to the posterior pharyngeal wall, and a few cases have been recorded of the tube being passed deep to the pharyngeal mucosa (Coffin, 1950). This seems the more likely to occur if the tube is firmly gripped in its passage through the nose and the "feel" of it lost.

Occasional laryngeal granulomata have also occurred following intubation (Gould, 1935).

In a perusal of sundry articles on intubation, one is struck by the lack of reference to the local preparation of the nose. In order to gain as much space as possible in a relatively small cavity, it seems only reasonable to use a vaso-constrictor (and preferably analgesic) preparation such as cocaine 10 per cent and adrenaline 1 in 4,000. This may be sprayed into the nares, or, if considerable difficulty is expected on account of deformity of the septum or turbinates (a not uncommon occurrence), the nose should be prepared with pledgelets of cotton wool soaked in the above solution. In this connection, the nose will usually have been examined by the surgeon, and his findings on the case sheet often give a valuable clue as to which nostril will prove the more patent.

Anaesthetic Technique.

The premedication prescribed was morphia gr. 1/6 (10 mg.) and atropine gr. 1/100 (0.65 mg.)—a compromise. Eighty-seven cases were anaesthetized with endotracheal ether as the main anaesthetic agent, following a nitrous oxide induction (table II). This generally gave good results although the induction took a little time.

In 17 cases chloroform was used in the Boyle's machine. It should be stated at this point that while the practice of dis-

secting tonsils in the adult is now almost universal, one is still occasionally asked to anaesthetize an adult for a guillotine tonsillectomy. If this is to be at all successful, full relaxation of the muscles concerned is essential, followed by a rapid return of the cough reflex. Nitrous oxide, oxygen and chloroform provide excellent operating conditions for this short procedure, which accounts for some of the 17 cases. The remainder were intubated under chloroform and dissection performed.

One of these cases deserves special mention. After intubation and connecting up the apparatus it was noticed that respiration had ceased. The pulse was impalpable. The pupils were dilated. The patient was, however, a good colour. One could not say definitely that the heart had stopped (for no time was spent on auscultation) but there was little evidence of its activity. The patient was placed in a steep Trendelenberg position immediately and inflated with oxygen. In just under one minute—it seemed longer—the pupils first became smaller, then the carotid pulse returned. Respiration resumed shortly thereafter and the pulse became full and regular. The patient's colour remained good throughout. Recovery was uneventful. It is considered that this may have been a case of primary cardiac failure, possibly precipitated by intubation.

The final blow against the use of chloroform, which tends to linger on in anaesthesia for throat surgery, was struck by the advent of the short acting muscle relaxants. The last 47 cases in this series were anaesthetized with thiopentone, suxamethonium (Scoline), nitrous oxide, oxygen and trichlorethylene. In a few cases a little ether was added if the operation was prolonged.

Suxamethonium belongs to that group of muscle relaxants which act by depolarization of the motor end-plate. This produces an initial stimulation and twitching of the muscle before paralysis ensues. In the conscious patient this is a painful process, and even when a small dose of thiopentone has been given, patients have complained of post-operative aching in muscles quite unrelated to the site of operation. The relationship between suxamethonium and muscle pains has been the subject of a recent study (Churchill-Davidson, 1954), which indicated that pain occurred chiefly in out-patients, and that its incidence and severity were reduced by abolishing the fascicular twitching which follows the injection. It would seem reasonable therefore to 'cover' the suxamethonium with an adequate dose of thiopentone, say, in the ratio of 10 mg. of thiopentone to each 1 mg. of suxamethonium. The average dose used was 650 mg. of thiopentone followed by 68 mg. of suxamethonium administered from a separate syringe.

After the nose has been sprayed, the patient's lungs are inflated with oxygen; when the jaw is fully relaxed, the tube is passed through the nose and one, or at most, two attempts at "blind" intubation made. Apnoea, if it occurs, is considered no disadvantage during this manoeuvre, as it is a simple matter to decide whether the tube is in trachea or oesophagus by having an assistant squeeze the chest. If the trachea is not readily entered it is considered no disgrace to insert the laryngoscope and introduce the tube under direct vision, using Magill's forceps if necessary.

The Boyle-Davis gag is then inserted by the surgeon and the throat packed. The head of the table is now dropped so that the patient's neck is in a position of hyperextension and any blood which escapes the sucker will pool in the naso-pharynx.

If hyperextension is extreme, however, a rubber tube may become kinked over the inter-arytenoid fold.

By the time the surgeon is ready to commence, respiration is usually adequate and trichlorethylene must be brought in early to prevent the patient straining on the tube (which is lubricated with a non-analgesic preparation). The duration of effect of the suxamethonium was found to be 2–5 minutes and no case of prolonged apnoea occurred although a dose of 100 mg. was used in a few cases.

At the conclusion of the operation when haemostasis is effected the surgeon removes his pack. An early return of the pharyngeal reflex is assured by maintenance of anaesthesia on nitrous oxide and oxygen alone during the latter part of the operation. The endotracheal tube is now withdrawn into the pharynx and removed from there with the sucker attached thus catching any blood clot which has accumulated in the naso-pharynx during operation. The patient is then turned on to his left side and returned to bed in that position. Pethidine (100 mg. intramuscularly) is preferred for post-operative sedation.

SUMMARY

The operative requirements and anaesthetic techniques used for tonsillectomy in children and in adults during 1948–53 are described. Whereas in children there has been little change in the anaesthetic technique employed, in adults, on the other hand, this has undergone considerable modification since the advent of the short acting muscle relaxants.

ACKNOWLEDGMENTS

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ANAESTHESIA FOR INTRA-NASAL AND INTRA-ORAL OPERATIONS IN ADULTS

Trial of a technique based on Intravenous Pethidine

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THE numerous different anaesthetic techniques in common use for intra-nasal and intra-oral surgery in adults reflect the diversity of opinion on this subject. With skilled administration the various methods yield satisfactory results though, perhaps, they may not possess all the desirable properties.

The most popular sequence is thiopentone followed by a relaxant, endotracheal nitrous oxide, oxygen and trichlorethylene, and in expert hands is very satisfactory. But if the induction dose of thiopentone is reduced to a minimum in order to ensure a rapid recovery of reflexes tachypnoea is a possible complication (Dundee, 1953), whilst a dose large enough to prevent this may cause delayed recovery. Also, unless the trichlorethylene is used in small quantities and withdrawn altogether before the end of a long operation delayed recovery may easily be produced (Ostlere, 1953).

This basic technique can be modified for use without intubation for tonsillectomy in association with regional analgesia and in the presence of an active cough reflex (Kenton and Parsons, 1953); or thiopentone may be used as the sole agent in the non-intubated patient (Griffiths, 1950a). In both these cases especial care must be taken to prevent aspiration of blood and the surgeon must be prepared to operate under such conditions.

Again, the trichlorethylene may be replaced by ether or cyclopropane, though these agents are inflammable and tend to cause increased post-operative nausea and vomiting. Ether may be used by insufflation on a Davis-Boyle gag for intra-oral operations; this technique though admirable for children is less satisfactory in adults since it may be difficult to maintain adequate anaesthesia. Muscle-relaxants can be employed to supplement thiopentone and endotracheal nitrous oxide and oxygen, but here the rapid recovery of consciousness is often associated with early pain and restlessness.

Consideration of the problems involved suggested that the ideal anaesthetic for this type of surgery is one which is non-inflammable, provides a pleasant rapid induction with easy atraumatic intubation of the larynx, and sedates the laryngeal and pharyngeal reflexes but allows of their rapid return at the end of operation. If possible it should provide a quick return to consciousness with freedom from excitement and early pain.

The very satisfactory conditions obtained in general surgery with nitrous oxide and oxygen anaesthesia supplemented with intravenous pethidine suggested that this sequence might be of value

in intra-nasal and intra-oral surgery if it could be demonstrated to be a safe procedure. Recent work has shown that pethidine can produce depression of respiration and the associated reflexes in a similar way to morphine. The respiratory depression caused by pethidine is one of rate rather than depth (Blazeby, 1951; Griffiths, 1950b), and Ruben and Andreassen (1951) have shown that pethidine is a sedative to the laryngeal and pharyngeal reflexes. Indeed, Ruben and Gammeltoft (1953) describe the performance of oesophagoscopy and gastroscopy under pethidine analgesia alone.

On these grounds it may be thought dangerous to use pethidine in operations following which there is liable to be blood in the vicinity of the larynx. The purpose of the investigation to be described was to determine whether it is desirable and safe to use pethidine and "light" anaesthesia for this type of surgery.

THE METHOD

Premedication.

Premedication is given 1½ hours before operation, i.e. papaveretum gr. 1/3 (20 mg.) and scopolamine gr. 1/150 (0.45 mg.), or morphine gr. 1/6 (10 mg.) and atropine gr. 1/100 (0.65 mg.), according to the patient's age and physique. Though there was no selection of cases most of the patients in this series were young and fit.

Induction of Anaesthesia.

A diaphragm needle is inserted into a vein on the dorsum of the foot and through this the minimum sleep-dose of thiopentone is injected *rapidly*. This varies between 3 and 6 ml. of the usual 5 per cent solution (150–300 mg.) depending on the patient's sex, age, physique, and the effect the premedication has had. Immediately the patient is asleep the mask is applied and a mixture of nitrous oxide 8 litres per minute, and oxygen 2 litres per minute (20 per cent oxygen) delivered on the semi-closed circuit; 250 ml. per minute of carbon dioxide may be added for a few minutes. Since significant nitrous oxide saturation of the tissues in the presence of adequate oxygenation takes at least 10–15 minutes, minimal trichlorethylene is added at this stage to ensure smooth anaesthesia. The reservoir bag is emptied at intervals during the operation in order to remove more quickly accumulated expired nitrogen.

After about two minutes, a mixture of an ultra-short-acting relaxant and an analgesic is injected intravenously, the respiratory rate serving as a guide to the dose of analgesic required. A choice of several combinations is available, viz.: suxamethonium chloride (Scoline, Anectine) 20–30 mg. active cation (25–38 mg. by weight or suxamethonium bromide (Brevidil M) 20–30 mg. active cation (30–45 mg. by weight) and pethidine hydrochloride 15–25 mg. or l-methorphinan (Dromoran) 1.0 mg.

Intubation.

When muscle fasciculation ceases the relaxed and apnoeic patient is ventilated several times by gentle pressure on the reservoir bag with the expiratory valve almost closed, and is then ready for intubation under ideal conditions.

(1) *Intra-nasal operations.* Oral intubation is performed under vision in the usual way. Adequate length of relaxation is present for the subsequent insertion of a pharyngeal pack.

(2) *Intra-oral operations.* Blind nasal intubation is performed with the head in the "sniffing the air" position. Generally the tube "falls" directly into the paralyzed larynx without any trouble, but occasionally it passes into the oesophagus, in which case further extension of the head and neck may lead to a successful intubation. If intubation again fails perfect conditions are still present for direct laryngoscopy and intubation with the aid of Magill endotracheal forceps.

The patient is now transferred to the theatre, i.e. 3–6 minutes from the first injection, but a slight delay occurs in transferring to the table and in "towelling up" so that operation begins 2–5 minutes later and by this time spontaneous respirations have returned. In intra-oral operations masseteric spasm occasionally occurs and makes difficult the insertion of the Davis-Boyle gag or dental props. This is best avoided by insertion of a gag before the action of the relaxant has worn off.

Maintenance of Anaesthesia.

When the operation commences the trichlorethylene is turned off and a maintenance mixture of nitrous oxide 5 litres per minute and oxygen 2 litres per minute (28.6 per cent oxygen) delivered. It is desirable that the largest tube possible is used so as to give a good fit in the larynx. Further doses of pethidine, e.g. 10–15 mg. (or 0.5–1.0 mg. l-methorphinan) are injected as necessary. A reliable indication for more analgesic was found to be a change in rate and/or depth of respirations, or breath-holding, both warning that coughing on the tube may soon occur unless more analgesic is given. Sudden movements of the head may initiate coughing and should be prevented by the use of carefully placed sandbags. If the head must be rotated this should be done slowly and gently. With carefully-timed repeat doses of analgesic a smooth anaesthesia is obtained without undue respiratory depression, but if doubt exists the respirations are assisted for short periods. Nalorphine may prove useful in accidental overdosage of analgesic (Eckenhoff, Elder and King, 1952), but was not required in this series.

Recovery.

As soon as the operation is completed the endotracheal tube is disconnected from the machine so that the patient is breathing air. Pharyngeal toilet is performed and great care taken to ensure that all packs and swabs have been removed. This is an essential step as the analgesic used during the operation may reduce pharyngeal sensitivity to packs even in the conscious patient (Report of Morbidity Conference, 1953).

The patient is placed in the semi-prone position and the endotracheal tube removed, i.e. about 1 minute after completion of operation. Extubation is accompanied by coughing or swallowing in all cases. The patient is transferred to a trolley and at this stage many regain consciousness. They obey simple orders, show no excitement and do not complain of pain from the operation site. Once back in bed many of them fall off into a short natural sleep but are in control of their own airway. Since the laryngeal and pharyngeal reflexes are present, the patients tend to swallow any blood that

oozes into the mouth after the operation, and this may cause vomiting later.

Though the residual action of pethidine gradually wanes, it tides the patient over the early post-operative hours in which restlessness is most likely to occur. Potent analgesics, therefore, are seldom required (only four patients required pantopon for mild restlessness) and later on aspirin gargles or tablets provide adequate relief in almost all cases. However, all tonsillectomy cases were routinely written up for post-operative morphine and this was not withheld later if required. In only one case (removal of a large dental cyst involving the maxillary antrum) was there marked restlessness and disorientation on awakening in theatre at the end of operation, and this occurrence was quite exceptional.

Specimen Cases.

In order to obtain accurate figures, sixty cases early in the series were timed on a stop-watch. The following examples show the records kept:

Intra-oral operation: Fit male, aet. 21. Tonsillectomy by dissection.

Min.	Sec.	
0	0	Diaphragm needle inserted.
0	8	Thiopentone mg. 250→N_2O 8l/O_2 2l + minimal trichlorethylene.
2	30	I.V. pethidine mg. 25 + suxamethonium Cl. mg. 35 by weight.
4	0	Blind nasal intubation—easy.
5	30	Into theatre.
8	0	Operation begins. N_2O 5l/O_2 2l. Trichlorethylene off. Respirations 14/min. Pethidine mg. 15.
12	0	Respirations 12/min. but deeper. Pethidine mg. 10.
17	0	Respirations 14/min.
19	30	Operation ends. Disconnect from machine.
20	10	Extubate with cough.
21	30	Conscious, quiet and co-operative.

There was no coughing on the tube during operation, aspirin gargles only were required, and there was no post-operative vomiting.

Intra-nasal operation. Fit male, aet. 23. Submucous resection.

Min.	Sec.	
0	0	Diaphragm needle inserted.
0	5	Thiopentone mg. 250→N_2O 8l/O_2 2l + minimal trichlorethylene.
2	0	I.V. pethidine mg. 25 + suxamethonium Br. mg. 35 by weight.
4	40	Oral tube and pack in.
6	0	Into theatre.
10	0	Operation begins. N_2O 5l/O_2 2l. Trichlorethylene off. Respirations 12/min. and deep. Pethidine mg. 10.
17	0	Respirations 14/min. and deeper. Pethidine mg. 10.
38	0	Respirations 13/min. and suddenly deeper. Pethidine mg. 10.
53	0	Respirations 14/min.
56	0	Operation ends. Disconnect from machine.
57	0	Pharyngeal toilet, pack out. Pharyngeal movements on removing pack.
58	15	Extubate with cough.
59	45	Conscious, quiet and co-operative.

There was no coughing on the tube during operation. Post-operatively there was frontal headache (?from nasal packs) and one vomit of stale blood.

RESULTS

The sequence has been used in 222 consecutive and unselected cases with nine different surgeons (table I). All patients were adults with the exception of six, aged 13–18 years, who, on account of their build were treated as adults. At the request of one surgeon general anaesthesia was combined with the method of topical

TABLE I
Operations performed with the technique

Intra-oral:	
Tonsillectomies by dissection	75
Dental operations	52
Intra-nasal:	
Submucous resections	36
Antrostomies	29
Caldwell-Lucs	9
Manipulations of fractured nose	7
Miscellaneous	14
	222

analgesia described by Moffett (1947) for a series of 30 nasal operations. This produced virtually a bloodless operative field.

Sleep-doses of thiopentone were used for induction of anaesthesia and figure 1 shows the doses used.

Pethidine was used in 202 cases (fig. 2), and l-methorphinan in 20 cases. Control

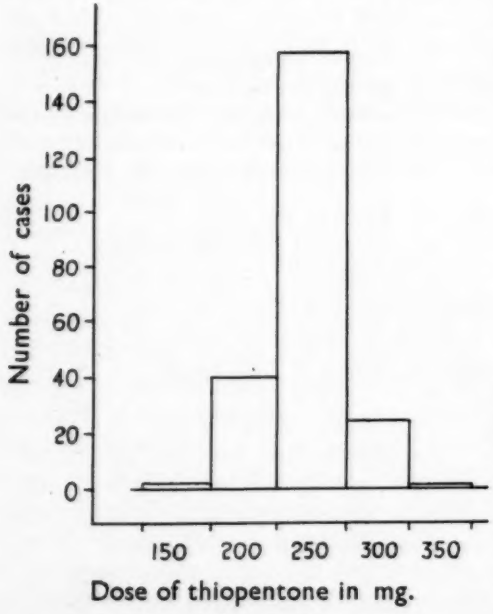

FIG. 1
Histogram showing dose of thiopentone used in 222 cases.

of analgesia during operation was found to be easier with pethidine than with l-methorphinan, as it was not so easy to give small doses of the latter drug and yet produce a noticeable effect.

In all intra-oral operations blind nasal intubation under suxamethonium relaxation was attempted unless contra-indicated (table II). If unsuccessful the

TABLE II
Details of attempts at blind nasal intubation under Suxamethonium relaxation

Number attempted	Successful	Unsuccessful	Success rate
126	106	20	84 per cent

method was not persisted in and direct laryngoscopy was performed.

The details of the anaesthesia of 60 cases early in the series were recorded with the aid of a stop-watch, and table III shows some of the figures obtained. In these cases duration of anaesthesia varied from $10\frac{1}{2}$ to 162 minutes.

TABLE III
Further details of 60 anaesthesias recorded with the aid of a stop-watch

Average induction time	Cough on extubation	Swallowing on extubation	Awake within 5 minutes
(min.)	(per cent)	(per cent)	(per cent)
$4\frac{1}{2}$	95	100	73

The "induction time" in the above table was measured from the moment of the first injection to the time that the patient was ready to be taken into the theatre. As an example that induction was not unduly prolonged, on one occasion a list of four tonsillectomies and one case of bilateral intra-nasal antrostomy was completed comfortably in $1\frac{1}{2}$ hours.

The post-operative vomit rate was 39 per cent.

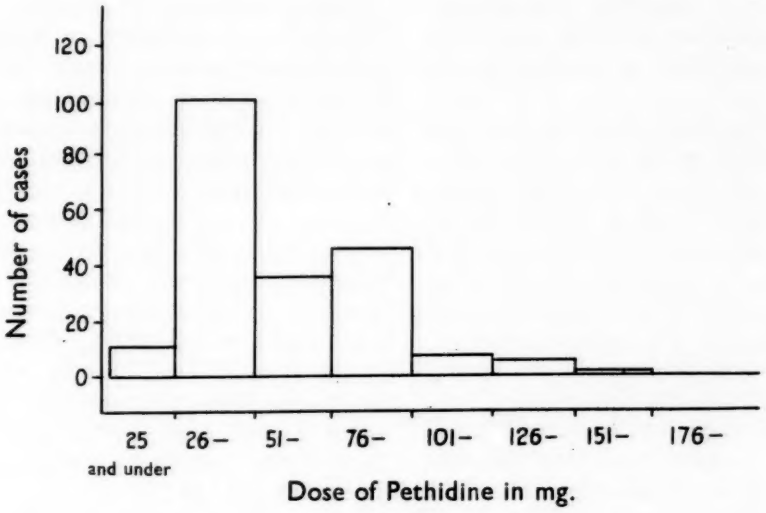

FIG. 2
Histogram showing dose of pethidine used in 202 cases.

Coughing on the tube during operation occurred in 10 per cent of cases early in the series, but with greater experience of the method this was later reduced to 4 per cent. There were definite contributory reasons in some cases, e.g. excessive movements of the head and neck in Caldwell-Lucs, slipping of the pharyngeal pack in one case of antrostomy, and a very long epiglottis in one tonsillectomy that was stimulated each time the sucker was used. This is commented on in the discussion.

Post-operatively analgesic injections were required within the first four hours in five cases; four of these for mild restlessness and one for severe restlessness.

There were no post-operative chest or other serious complications in the complete series, though a number of patients had a sore throat from the pharyngeal pack.

DISCUSSION

The sequence just described will now be discussed in detail.

Sleep-dose of Thiopentone. Many anaesthetists regularly employ doses larger than the 150 to 300 mg. required to produce sleep. Indeed, Griffiths (1950a) described the use of thiopentone as the sole agent for tonsillectomy in adults and stated that "most patients recovered consciousness within 20–30 minutes of returning to bed, after which they usually fell into a sleep lasting up to 3, or even 4 hours."

However, in this investigation a single sleep-dose was preferred, so as to allow rapid recovery after the anaesthesia. This is in agreement with the suggestion of Lief et al. (1952) that "barbiturates should be considered as basal hypnotic agents in clinical anaesthesia rather than anaesthetic agents, since these drugs

possess limited analgesic and muscle-relaxant properties and do not yield sufficient depression of autonomic reflexes."

Intubation. Intubation offers several advantages over insufflation on the Davis-Boyle gag. Easier control of anaesthetic depth is obtained, and a perfect airway free from the dangers of aspiration and laryngospasm is possible. Finally most intra-nasal and intra-oral operations may be performed in the intubated patient, whereas insufflation methods are applicable only to intra-oral operations.

The satisfactory use of relatively small doses of suxamethonium to produce relaxation has been discussed elsewhere (Franks, 1953).

Ruben and Andreassen (1951) have shown that the combination of pethidine, a relaxant, and nitrous oxide and oxygen is a useful technique in intubation under "light" anaesthesia. Their findings have been verified in this series of cases.

In a search of the literature I have found no previous reference to blind nasal intubation of the larynx under suxamethonium relaxation. Many anaesthetists consider that blind nasal intubation is now no longer necessary or desirable, but as Nosworthy (1953) points out, "Every now and then, however, the blind method provides the answer to an awkward situation". For this reason it would be a loss if the method fell into complete disuse. This series included three cases of dental surgery in recently fractured mandibles, and blind nasal intubation was considered to be the method of choice. In order to gain experience of the method it would appear that suxamethonium is extremely useful.

Maintenance of Anaesthesia. The combination of pethidine and trichlorethylene to supplement nitrous oxide and oxygen anaesthesia to a large extent abolishes the disadvantages of either drug used alone. Johnstone (1951) summarized his findings thus: "... the use of pethidine in conjunction with nitrous oxide, oxygen and trichlorethylene is advocated as a safe and satisfactory method of anaesthesia for operations not requiring profound muscular relaxation". With pethidine alone it is difficult in some patients to obtain complete analgesia; recourse to supplementary doses of thiopentone or a relaxant may then be necessary to obtain smooth anaesthesia.

With careful use of the two drugs adequate analgesia is obtained without either tachypnoea from excess trichlorethylene or severe respiratory depression due to pethidine. It was considered that, in the presence of moderately deep respirations of 12–16 per minute, and an oxygen-rich mixture (28.6 per cent oxygen), anoxia does not occur. This agrees with Bourne (1953) who recommends, in cases of prolonged apnoea following suxamethonium, artificial respiration with nitrous oxide and oxygen on the semi-closed circuit at a rate of 12–15 per minute in an attempt to "imitate the breathing movements that might be imagined if the patient were lying quietly asleep."

It may well be desirable in future to use rather more trichlorethylene with consequent reduction in the dosage of pethidine. This would provide a slightly "deeper" anaesthesia with less likelihood of coughing or swallowing on the tube during operation.

Recovery. Extubation was accompanied by a cough or swallowing in all cases and, therefore, there was no evidence that at the end of operation the cough reflex was dangerously depressed even in the relatively high total dosage used. The theoretical objections to the use of respiratory depressant drugs for this type of surgery were mentioned in the introduction to this paper and this investigation has shown that such drugs may be used with safety if care is taken. Albeit, topical analgesia of larynx and trachea combined with inhalation anaesthesia for this type of surgery would appear to be open to the same objections, yet its use is described by some workers (Bourne, 1954). In the technique described in this paper the cough reflex is completely obtunded only for a short period during and immediately following intubation, and thereafter it is merely sedated. In this lies the safety of the method as shown by the complete absence in the whole series of post-operative complications referable to the inhalation of blood.

Wolfers (1953) demonstrated that statistically there is a significantly higher post-operative vomit rate when intravenous pethidine is used during anaesthesia than in otherwise similar techniques in which it is avoided. This may account for the high figure (39 per cent) found in this investigation. However, most of the vomits contained altered blood, and it is thought that this may have been an important contributory factor. It was noticed that vomiting tended to follow the first post-operative drink even if this was not taken till 6 or 10 hours after operation. In no case was vomiting persistent or exhausting.

Johnstone (1951) observed that following pethidine with trichlorethylene, analgesia is well marked for three or four hours after operation. These findings were confirmed for pethidine, as were those of Brown (1952) and Brotman, Cullen and Wilkins (1950) for l-methorphinan. The rarity of post-operative restlessness associated with the rapid return to consciousness following the exhibition of these drugs would appear to be directly related to this residual action.

CONCLUSIONS AND SUMMARY

An investigation is described which was undertaken in order to determine whether intravenous pethidine (or l-methorphinan) has any place in anaesthesia for intra-nasal and intra-oral in-patient operations in adults. A technique for its administration is described and discussed in detail. The method, which has been used in 222 consecutive and unselected personal cases with nine different surgeons, has proved satisfactory to the patient, surgeon, anaesthetist and nursing staff.

The conclusion reached is that intravenous pethidine is a useful and safe anaesthetic adjuvant for this type of surgery in adults if care is taken.

Blind nasal intubation of the larynx under suxamethonium relaxation is described, and its place in modern anaesthetic practice discussed.

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MANCHESTER MEDICAL SOCIETY

SECTION OF ANAESTHETICS: SESSION 1954–55

1954			
October	21:	Presidential Address: Dr. A. R. Hunter	"Hyperglycaemia, acidosis, and ketosis in anaesthetized patients."
November	18:	Dr. A. Earnshaw	"Kinking of Endotracheal Tubes."
		Dr. R. W. Buckley	"The Depression of Respiration by Pethidine during Anaesthesia."
1955			
February	17:	Dr. T. H. Chadwick	"Anaesthesia for Prostatic Surgery."
March	17:	Dr. Geoffrey Organe	(Title to be announced later.)
April	21:	*Joint Meeting with the Liverpool Society of Anaesthetists*	
		Dr. M. Johnstone	"The Mechanisms of Cardiac Arrest."
		Dr. G. McLoughlin	"Haemostasis."

Summer meeting to be held in Preston and organized by Dr. A. J. Gray. Date to be arranged later.

Brit. J. Anaesth. (1954), **26**, 427.

PROLONGED APNOEA FOLLOWING SUXAMETHONIUM CHLORIDE

BY

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SINCE the introduction into clinical practice of the ultra-short-acting relaxant suxamethonium chloride there have been a number of reports of prolonged apnoea attributed to its action.

Before apportioning blame care must be taken to differentiate between apnoea due to muscular paralysis and that caused by the central effect of such respiratory depressants as morphine, thiopentone and pethidine, given individually or in combination. Taking this into consideration, however, enough has been published, notably by Hurley and Monro (1952), Hewer (1952), Love (1952), Harper (1952), Forbat, Lehmann and Silk (1953), Harrison, Seward and Skinner (1954) and Cowan (1954), to establish that suxamethonium may give rise to paralysis prolonged beyond its normal limits. Such abnormal prolongation rarely exceeds half an hour, but Cowan (1954), has reported a case in which apnoea lasted for over nine hours.

The mode of action of suxamethonium and its fate in the body would lead one to expect in these cases a significant lowering of the serum-cholinesterase level, and this has been shown to exist by Bourne et al. (1952), Evans, Gray, Lehmann and Silk (1952), and Forbat, Lehmann and Silk (1953).

A low serum-cholinesterase level may be caused by severe liver disease, malnutrition and exposure to the organic insecticides and weed killers, but it may also occur in the absence of these conditions.

The treatment of prolonged apnoea due to suxamethonium includes the maintenance of adequate respiration, the continuance of light anaesthesia to guard against return of consciousness during the period of paralysis, and transfusion of whole blood or serum to replace the deficient serum-cholinesterase. Neostigmine tends to prolong paralysis by its action on cholinesterase and is contra-indicated.

The following two cases of suxamethonium sensitivity, occurring in childhood and old age, are interesting as in neither was there anything clinically to suggest the low serum-cholinesterase levels which were found on subsequent blood examination. In the child apnoea lasted for forty-five minutes, in the old woman for nearly five hours.

CASE I

A boy aged 8 years was admitted to hospital following the unsatisfactory reduction in the Casualty Department of a fractured right radius and ulna. He appeared a normal healthy child. Weight 50 lb. (22.7 kg.). No history of previous illness.

6.25 p.m. Premedication: papaveretum 11.0 mg., scopolamine 0.22 mg.

7.15 p.m. Induction: thiopentone 300 mg. Maintenance: nitrous oxide 5 litres/min. and oxygen 2 litres/min. by the semi-closed method, and minimum trichlorethylene.
7.20 p.m. Respirations well established. Suxamethonium 25 mg. Rapid relaxation. Fracture reduced and immobilized after check X-rays.
7.35 p.m. Apnoea persisting.
7.50 p.m. Still completely apnoeic.
8.5 p.m. Feeble voluntary respirations returning, diaphragmatic in character.
8.10 p.m. Respirations well established.
8.45 p.m. Recovered consciousness.

He made an uneventful recovery and appeared none the worse for his experience. Blood examination showed a low serum-cholinesterase level: serum-cholinesterase activity: 70 micromols/ml. /hr. (normal 130–310). Repeated one month later: 50 micromols/ml./hr.

CASE II

A woman aged 84 years was admitted to hospital with a sub-capital fracture of the left femur. Her condition was poor. Incontinent of urine. Pulse irregular. Moist sounds at both bases. Estimated weight 170 lb. (77.2 kg.). B.P. 170/82. Hb 85 per cent Sahli. In view of her general condition it was decided to facilitate nursing and obtain early mobility by the insertion of a Smith Petersen pin.

4.30 p.m. Premedication: atropine 0.64 mg., pethidine 50 mg.
5.20 p.m. Induction: thiopentone (2½ per cent soln.) 200 mg., suxamethonium 50 mg. No. 9 orotracheal tube passed. Maintenance: nitrous oxide 6 litres/min. and oxygen 2 litres/min. by the semi-closed method, supplemented by pethidine 25 mg.

Throughout the operation her condition was satisfactory. Colour good. Pupils moderately contracted. Pulse rate 80/min., regular but soft. There was a striking absence of bleeding at the operation site. Voluntary respirations, however, did not return.

6.00 p.m. Operation completed. Still apnoeic. Nikethamide 5 ml. intravenously.
6.30 p.m. P.R. 90/min. B.P. 170/80. During the next half-hour she received nalorphine 40 mg. in divided doses.
7.15 p.m. P.R. 90/min. B.P. 170/80. Blood transfusion started.
7.30 p.m. Anaesthetic discontinued. Still complete apnoea. She appeared to be deeply unconscious. Larynx insensitive to stimuli. Respirations maintained by a Bragg Paul Pulsator, supplemented by intratracheal oxygen. Colour good. Returned to the ward.
8.45 p.m. P.R. 128/min. Resp. rate 24/min. B.P. 170/86.
10.00 p.m. P.R. 128/min. Resp. rate 24/min. B.P. 140/76. Still complete apnoea.
10.15 p.m. Slight movement of right leg noticed.
10.30 p.m. Pulsator switched off and voluntary respirations found to be well established. Pulsator discontinued.
10.45 p.m. P.R. 136/min. Resp. rate 20/min. B.P. 90/?
11.30 p.m. P.R. 86/min. Resp. rate 20/min. B.P. 80/?
12.30 a.m. P.R. 110/min. Resp. rate 20/min. B.P. 84/?
3.30 p.m. P.R. 86/min. Resp. rate 20/min. B.P. 94/? She regained consciousness.
10.30 a.m. P.R. 90/min. Resp. rate 24/min. B.P. 160/70.

She sat up in bed, but for the next few hours experienced slight difficulty in coughing and swallowing. Considering her pre-operative condition she appeared remarkably well. She made satisfactory progress and developed no chest complications.

Blood estimation three days later showed a low serum-cholinesterase level. Serum-cholinesterase activity: 45 micromols/ml./hr. (normal 130–310).

DISCUSSION

In neither of these cases can prolonged apnoea have been due to thiopentone or narcotics. In the child, respirations were established before the injection of suxamethonium. In the adult the small induc-

tion dose of thiopentone did not produce apnoea, and it would be difficult to attribute respiratory depression of five hours duration to the supplementary dose of pethidine. She showed no sensitivity to it when it was given pre-operatively for pain, and later for premedication. It is unlikely that acapnia played any part in either case, as the absorber was not used.

In view of the small quantity of anaesthetic used, it is difficult to explain the delayed recovery of consciousness in Case II—some eight hours after the discontinuance of gas and oxygen and nearly five hours after the return of voluntary respirations. On subsequent questioning she could remember nothing between the time of induction at 5.20 p.m. and 3.30 a.m. the following morning. Cowan (1954) has noted delayed recovery of consciousness in a patient in whom apnoea persisted for nine hours, but in this case recovery coincided with the return of respiration.

An interesting feature of Case II was the absence of bleeding, so striking as to be compared by the surgeon with controlled hypotension produced by hexamethonium bromide. It is unfortunate that no blood pressure readings were taken at the time. The post-operative B.P. was 170/80 mm. Hg, but this was after nikethamide had been given, and half an hour after the completion of the operation. Lehmann and Silk (1953) have shown that succinylmonocholine, a breakdown product of suxamethonium, produces, in rabbits, a hexamethonium-like effect on peripheral blood vessels accompanied by "pooling" of blood in dependent parts of the body. The paralysant effect is prolonged.

As regards the dose of suxamethonium used, I have found 0.5 mg. per lb. (0.45 kg.) body weight to be generally satisfactory in a series of some two hundred children under twelve years of age. In two cases, however, relaxation though profound was too transitory to allow unhurried intubation. There is some evidence that the length rather than the depth of paralysis is proportional to the amount of suxamethonium injected. At the other end of the scale, the aged tolerate the drug well, and a standard dose of 50 mg. can be given, irrespective of age or weight. In a series of sixty-six operations for fracture of the neck of the femur in patients between seventy and a hundred years of age the average period of apnoea produced by this dose was no longer than in a comparable series of young adults.

As sensitivity to suxamethonium is generally due to a low serum-esterase level, blood transfusion is indicated. Harrison, Seward and Skinner (1954) attributed the return of respirations in prolonged suxamethonium apnoea to transfusion of fresh blood. Cowan (1954) reports a dramatic response to fresh blood after a failure of older blood. A blood transfusion was given to Case II, but it is difficult to say how much this effected the eventual recovery of muscle tone.

SUMMARY

Two cases of prolonged apnoea following the administration of suxamethonium chloride are reported. In a child of 8 years apnoea persisted for 45 minutes, in a woman of 84 years for nearly 5 hours. Both subsequently showed low pseudocholinesterase levels. Neither appeared to suffer any ill effects, and it would seem that such fortunately rare occurrences

are more of an embarrassment to the anaesthetist than a danger to the patient.

ACKNOWLEDGMENT

I have to thank Dr. G. A. James of the Pathological Department, Hastings Group of Hospitals, for carrying out the serum-cholinesterase estimations in these patients.

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BOOK REVIEW

A.M.A. Fundamentals of Anaesthesia (3rd edition). By the Councils and Bureaux of the American Medical Association. Published by W. B. Saunders Co. Ltd. Price £1 10*s*.

This book contains 300 pages and 89 illustrations together with 19 tables. The illustrations are more remarkable for their clarity than their beauty. In the preface the following paragraph occurs: "The necessary brevity of *Fundamentals of Anaesthesia* perforce makes it appear dogmatic. However, an effort has been made to dwell on principles at the expense of detail. Methods of treatment and dosage schedules suggested cannot be considered as 'routine' as each patient presents individual problems. It should also be remembered that the choice of drugs and technics is secondary to their judicious and skilled application."

If this paragraph is kept in mind we can say without hesitation the Committee on Revision has done its work well and achieved its object. It is not a book to read but one to which to refer. It should prove useful to examiners for it provides them with innumerable questions and to students for it supplies them with all the answers. The chapters on the 'Physiology of Respiration' and on 'Chemistry and Physics' will help the technician to become an anaesthetist. The amount of space allotted to regional analgesia is surely out of all proportion to the importance of the subject, or at least to the relative number of operations done under general anaesthesia on the one hand, and under local on the other. There seems to me a good deal to be said for dealing with the subject of 'Anaesthesia' in two separate volumes, one for local and one for general anaesthesia.

The metric system is used exclusively for the doses of drugs, and so we have 16 mg. for $\frac{1}{4}$ gr. For those of us who are more used to the old system a definite effort of translation has to be made every time a dose is mentioned. There are a number of tables in the appendix, useful certainly, but scarcely necessary to tell us that a milligram equals 0.001 gram. On the other hand the list of ampoules that may and may not be autoclaved is right up to date. The print and paper are both excellent.

E. Falkner Hill

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ANNOTATION

E.N.T. ANAESTHESIA

OPERATIONS on the nose and throat depend for their ease of accomplishment and safety on the skill of the anaesthetist. Deaths still occur during tonsillectomy from asphyxia due to a blood clot in the trachea; during mastoid operations in a darkened theatre from respiratory obstruction and from shock after laryngectomy (Mushin, 1946). Deaths also occur during oesophageal and bronchoscopic examinations. In 1896 Hewitt wrote, "Why do not deaths from anaesthetics show signs of diminishing? The reply is that the responsibilities involved in administering anaesthetics are not fully realized and that the administration is too often placed in the hands of comparatively unskilled men. . . . The first step should be an educational one." The problem remains; the solution is probably the same and the articles in this issue of the *British Journal of Anaesthesia* may serve to draw attention to one aspect of anaesthesia which has tended to be rather neglected and be overshadowed by more dramatic advances in other directions.

Today, with cuffed endotracheal tubes and the use of less toxic anaesthetic drugs the picture would appear to be much improved when compared with the beginning of the century. In 1907 Boyle wrote that laryngotomy should be performed for operations on the tongue or jaws and anaesthesia maintained by administering chloroform through the laryngotomy tube. He also considered that a feather should be used to remove mucus and blood from the trachea!

The problems posed by anaesthesia for otolaryngological surgery are:

(*a*) The maintenance of a clear and efficient airway without obstructing the surgeon.

(*b*) The prevention of excessive bleeding; the commonest causes are:

(i) Respiratory obstruction and hypoxia.

(ii) Straining due to active reflexes.

(iii) Hypercapnia due to respiratory depression either from drugs, pressure on the chest or excess carbon dioxide inhaled.

(iv) Obstruction to the venous return from the head usually caused by faulty positioning of the head.

(*c*) The prevention of the aspiration of blood, mucus, pieces of tonsil, polyps, packs and other foreign bodies.

(*d*) Rapid return of laryngeal reflexes at the end of the operation.

(*e*) Use of non-inflammable anaesthetic agents when diathermy is used.

In this journal Dr. Stirling describes the methods of anaesthesia for tonsillectomy used at the Glasgow Ear, Nose and Throat Hospital during the last five years. For guillotine and dissection tonsillectomy in children the nitrous oxide-oxygen-vinyl ether-ethyl ether anaesthetic sequence was considered the safest method. Because of the danger of psychic trauma (Annotation, 1954) nitrous oxide would

appear to be the anaesthetic of choice for induction. The alternative is to give a sleep dose of thiopentone, for example, 100–200 mg. intravenously (Bullough, 1952). Dr. Stirling does not mention the type of gag used in guillotine tonsillectomy. Deciduous teeth extracted by means of a mouth gag can give the surgeon and anaesthetist cause for concern. A side gag is preferable in this respect to a front gag.

In adult tonsillectomy the development of ultra short-acting relaxants has allowed ease of intubation with light anaesthesia and the quick return of reflexes. For intra-nasal and intra-oral surgery intravenous pethidine with nitrous oxide and oxygen has been used by Dr. Harvey Franks, who discusses this technique on another page. The main disadvantage appears to be the high incidence of postoperative vomiting. This is true of many modern anaesthetic agents—the only common drawback that a competent anaesthetist cannot entirely overcome is the possibility of sickness Dr. Franks states that there appears to be no delay in recovery of laryngeal reflexes in his cases, but it is well known from the work of Ruben and Andreassen (1951) that pethidine has a selective action on the larynx. It has been suggested (Johnson, 1951) that less pethidine would be used if administered in a continuous intravenous drip. This would tend to overcome the danger of giving too much pethidine and obtunding the laryngeal reflexes postoperatively with the danger of aspiration of vomit and debris.

It could be argued that were anaesthetists to pay as much attention to the problems involved in dealing with otolaryngological surgery in children and adults as they do to those of specialized cardiac surgery, more widespread good for the general community would follow.

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ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

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(*Continued from page* 342)

PHYSIOLOGICAL EFFECTS OF CHLOROFORM

Chloroform belongs to the large class of medicines known as narcotico-irritants. This and some other agents which have been inhaled for the prevention of pain are often called anæsthetics; a name to which there is no objection, so long as it does not lead to the idea that they have a different action from other narcotics, or more precisely speaking, narcotico-irritants; there being no such medicines as pure narcotics. The term anæsthesia has been frequently employed to designate the insensibility and suspension of consciousness caused by chloroform and ether; but, in describing the effects of these agents, I shall confine this term to its original meaning, privation of feeling, and I shall employ the term narcotism to designate the entire effects of these agents on the nervous system. This is the sense in which the term narcotism has always been employed. It has been the custom, however, to restrict the use of the word very much to cases in which stupor existed, but I shall apply it to designate the slighter, as well as the more profound effects of a narcotic, as I am entitled to do by strict etymology.

In order to facilitate the description of the effects of chloroform, I have been in the habit of dividing them into degrees. I use the term degree in preference to stage, as, in administering chloroform, the slighter degrees of narcotism occur in the later stages of the process, during the recovery of the patient, as well as in the beginning. The division into degrees is made according to symptoms, which, I believe, depend entirely on the state of the nervous centres, and not according to the amount of anaesthesia, which there is good reason to conclude, depends, in a great measure, on the local action of the chloroform on the nerves. The different degrees of narcotism glide insensibly into each other.

In the first degree, I include all the effects of chloroform that exist while the patient retains a perfect consciousness of where he is, and what is occurring around him. This degree constitutes all that a person remembers of the effects of the vapour, except when he happens to dream, and recollect it afterwards. The sensations caused by inhaling chloroform are usually agreeable, when it is taken merely for curiosity; and individuals who have inhaled nitrous oxide at some previous time

of their lives, often describe their feelings as being very much the same from both agents. Patients who are about to undergo a surgical operation are, however, not always in a state for receiving agreeable impressions, and they sometimes complain of palpitation of the heart, and a feeling of fulness in the head. There is generally a sense of dizziness, with singing in the ears and tingling in the limbs. Many persons have a feeling like that of rapid travelling, and as an appearance of darkness sometimes comes on from the failure of the sight, whilst there is also a loud noise in the ears, it not infrequently happens that a person feels as if he were entering a railway tunnel, just when he is becoming unconscious.

Those persons whose mental faculties are most cultivated appear usually to retain their consciousness longest whilst inhaling chloroform; and, on the other hand, certain navigators and other labourers, whom one occasionally meets with in the hospital, having the smallest possible amount of intelligence, often lose their consciousness, and get into a riotous drunken condition, almost as soon as they have begun to inhale. There is a widely different class of persons who also yield up their consciousness very readily, and get very soon into a dreaming condition when inhaling chloroform. I allude to hysterical females.

There is often a considerable diminution of the common sensibility during the first degree of narcotism by chloroform, more especially when it is inhaled very slowly, so that the patient is kept some minutes partially under its influence. In this way neuralgia can often be relieved, without removing the consciousness, when it is not extremely severe, and the suffering of labour may often be removed in the same manner, when the pains are not very sharp. In a few cases, the extraction of a tooth and other minor operations have been performed without pain, whilst consciousness has been retained; but as a general rule, it is better not to operate under these circumstances, for failure is more likely than success; and this plan does not succeed in any case without inhaling longer, and consuming more chloroform, than would be necessary in the usual way. The complete recovery of the patient from the effects of the vapour, after a protracted inhalation of this kind, is also more tardy.

The first degree of narcotism recurs when consciousness returns as the effect of the chloroform is subsiding. At this time, there is generally a greater amount of anæsthesia than at the commencement of inhalation, just before consciousness is removed. I have many times known the introduction of sutures, and such like measures, performed at the concluding part of an operation, after the patient had recovered his consciousness, without his feeling what was being done. As a general rule also, the smarting of the wound does not commence till some time after consciousness has returned.

In the second degree of narcotism, there is no longer correct consciousness. The mental functions are impaired, but not necessarily suspended. When a patient inhales chloroform quietly for a medical or surgical purpose, he usually appears as if asleep in this degree; but if his eyelid be raised, he will move his eyes in a voluntary manner. There are occasionally voluntary movements of the limbs;

and although the patient is generally silent, he may nevertheless laugh, talk, or sing. Persons sometimes remember what occurs whilst they are in this state, but generally they do not. Any dreams that the patient has, occur whilst he is in this degree, or just going into, or emerging from it, as I have satisfied myself by comparing the expressions of patients with what they have related afterwards. There is sometimes a little trouble with the patient in this degree of narcotism. He feels the inconvenience of the vapour he is breathing, and having become unconscious of the object for which it is inhaled, he endeavours to push away the inhaler. As a person in this condition can generally hear and partly understand what is said, a few kind words will often render him tractable. This is generally true of all those who have been brought up with care and kindness, more especially patients of the female sex; but the man who has been roughly treated from the time of his birth, can often be made insensible only by means of a little restraint.

There is generally a considerable amount of anæsthesia connected with this degree of narcotism, and I believe that it is scarcely ever necessary to proceed beyond it in obstetric practice, not even in artificial delivery, unless for the purpose of arresting powerful uterine action, in order to facilitate turning the fœtus. The loss of sensation is indeed sometimes so complete in this degree, especially in children, that the surgeon's knife may be used without pain; I have indeed seen a child unconsciously handling its toys all the time that the operation of lithotomy was performed on it. Commonly, however, the use of the knife, when the narcotism has not proceeded further than this degree, occasions expressions indicative of pain, which are either not remembered, or are recollected as having occurred in a dream. The patient is generally in this degree during the greater part of the time occupied in protracted operations; for although, in most cases, it is necessary to induce a further amount of narcotism before the operation is commenced, it is not usually necessary to maintain it at a point beyond this.

In the third degree of narcotism, there are no longer any voluntary motions. The eyes, for instance, are not directed towards any object; and although the limbs may move, they are not directed to any purpose. The pupils are generally inclined upwards in this degree, and are at the same time usually somewhat contracted. The blood-vessels of the conjunctiva are generally somewhat enlarged in this degree in all persons who are well nourished and not deficient in blood. It is in this degree of narcotism that rigidity and spasms of the muscles occur in certain cases. These phenomena occur most frequently in cases where the muscles have been much exercised, and are consequently well nourished. They are never met with in infancy, and rarely before puberty. They are much more common in the male than the female sex. The rigidity and spasm are greatest and most constant in labourers and persons accustomed to athletic exercises, and they are usually absent in patients who have been long confined to the room, or are much reduced in strength from any cause. They are less marked in old age than in the middle period of life, and they are not by any means so frequent or strong in fat, as in

thin, muscular persons. I have seen the spasms take an epileptiform character in a few cases; but by gently continuing the chloroform, they have always been subdued. In a great number of cases, the patient mutters in an almost inarticulate and a perfectly unintelligible manner, just as the muscular rigidity and spasm are subdued. Under these circumstances, I have never heard a single word pronounced so that it could be understood. If articulate language is uttered just after the muscular rigidity, it is evidence that the effects of the chloroform are being allowed to diminish, and that the patient is going back into the second degree of narcotism.

In the third degree of narcotism, a person is quite incapable of having any perception or consciousness of pain, but anæsthesia is not a necessary part of this amount of narcotism when it is first induced, and in some cases a patient may flinch, and put on an expression of countenance which seems indicative of pain. He may also cry out, but not in an articulate manner. By continuing the chloroform gently for a minute or so, a state of compiete anæsthesia can be induced in nearly every case, without carrying the narcotism of the nervous centres further than this degree. The loss of sensibility of the conjunctiva, as shown by the absence of winking when the edges of the eyelids are gently touched is the best criterion that the patient will bear the knife without flinching or crying.

The circumstance of the anæsthesia, or loss of common sensibility, not keeping pace with the degree of narcotism of the brain, as shown by the presence or absence of consciousness and volition, appears to depend on the chloroform acting on the peripheral distribution of the nerves, as well as on the nervous centres.* The following considerations support this view. 1. Chloroform has the effect of diminishing the sensibility of a part to which it is applied locally, even to the sound cuticle. When the cuticle is removed, the local anæsthesia of the surface is complete; and in frogs, which have a thin permeable skin, and a languid circulation, one limb can be rendered insensible, by the local application of this agent, before the remainder of the animal is much affected. 2. Chloroform when inhaled immediately circulates throughout the body, in all parts of which it can be detected by chemical means. 3. Chloroform and other narcotics suspend the function of the nerves, when locally applied to them. 4. When inhaled, the local effect of chloroform must be greatest when it has had time to exude through the coats of the vessels, into the extra vascular liquor sanguinis, and come into immediate contact with the nervous fibrillæ; and it must take some little time after the chief part of the chloroform has escaped from the blood during its passage through the lungs, before that which is in the lymph external to the vessels can pass back again into them, by endosmosis. The brain, on the other hand, is without lymph and lymphatics. The blood in this organ is all contained within the vessels, in which, moreover, it circulates with more velocity than in the external parts of the body. It can be easily understood, therefore, how the brain may escape from the effects of the vapour whilst the nerves of sensation

* Lancet, Feb. 12, 1848.

throughout the body still remain partially under its influence. 5. It is in young subjects, in whom, connected with the more active process of nutrition, the quantity of lymph external to the vessels is greatest, that the general insensibility most frequently remains, whilst the cerebral hemispheres are resuming their functions; whilst in persons of spare habit, approaching the middle or later periods of life, there is little anæsthesia except in the unconscious state.

The co-operation of the brain with the nerves is, of course, necessary to sensation; and it is possible by a large dose of chloroform to produce complete anæsthesia very suddenly, before there is time for the nerves to be acted on locally to any extent; and if the chloroform is not continued, the anæsthesia may subside as quickly as it was induced. The large ganglia of sensation, the optic thalami, seem to require a greater quantity of chloroform to suspend their function than is necessary to suspend that of the cerebral hemispheres, but, by occupying three or four minutes in giving chloroform, one is enabled to add its local action on the nerves to its influence on the brain, and thus to induce anæsthesia with less narcotism of the nervous centres than would otherwise be required.

It must not be supposed that the difference of the action of chloroform on the cerebral hemispheres, and on the optic thalami, will of itself explain the want of uniformity between the loss of consciousness and loss of feeling. If it were a mere difference of degree, it might be so explained; but the absence of all regular relation between these phenomena can only be satisfactorily accounted for when the circumstances connected with the circulation and the liquor sanguinis, that I have endeavoured to explain above, are taken into account.

In the fourth degree of narcotism, the breathing is stertorous, the pupils are dilated, and the muscles completely relaxed. The patient is always perfectly insensible. It is very seldom necessary to carry the effects of chloroform as far as this degree. It is, however, sometimes requisite to do so, in attempting to reduce dislocations of long standing in muscular persons, and whilst the surgeon is dissecting in the neighbourhood of important vessels and nerves, in certain robust subjects and others who seem to have acquired an excess of sensibility by hard drinking, and who can hardly be kept quiet under the knife, except when the breathing is stertorous.

There are some further effects of chloroform with which one becomes acquainted in experiments on the lower animals. If the inhalation is continued after the symptoms just described are produced, the breathing is rendered difficult, feeble, or irregular, and is sometimes performed only by the diaphragm, whilst the intercostal muscles are paralysed. If the dose of chloroform is gradually increased after these effects are produced, the breathing entirely ceases, but the heart continues to pulsate very distinctly, till its action becomes arrested by the absence of respiration, as in asphyxia. This interval, including the embarrassment and cessation of the breathing, I call the fifth degree of narcotism.

Although the respiration may be suspended by an amount of chloroform that has very little direct effect in the motion of the heart, it is quite possible to stop the

heart's action by the immediate effect of this agent. When frogs are exposed to the action of the vapour, they go on absorbing it by the skin, after the respiratory movements have ceased; and in this way the pulsations of the heart are arrested, when a certain amount of chloroform has been absorbed into the blood. And when animals of warm blood are made to breathe air containing as much as eight or ten per cent. of the vapour of chloroform, the blood which is passing through the lungs becomes so charged with it as to stop the action of the heart, when it reaches that organ through the coronary arteries. It is in this way that accidents from chloroform have happened. The power of this agent to arrest the pulsations of the heart can also be shewn, by blowing a stream of vapour on its surface, when the chest is opened immediately after the breathing has ceased, and whilst it is still beating.

The ultimate and greatest effect that chloroform is capable of producing on the animal body is to destroy the irritability of the muscles, and produce the post mortem rigidity. Either the whole body or a single limb can be rendered instantly rigid by injecting the arteries with a little chloroform shaken up with water. The rigidity remains for weeks in the dead body, and would probably be permanent if the chloroform were prevented from evaporating. Whilst it lasts, putrefaction is of course prevented.

Effect of Chloroform on the Pulse. I have not mentioned the state of the pulse in the above description of the effects of chloroform, for it affords no criterion of the amount of narcotism, and it was better therefore to reserve it for a separate notice. It is nearly always increased both in force and frequency, more especially at the early part of the inhalation. After the patient has become quite insensible, the pulse indeed generally settles down nearly to the natural standard, and in the middle of the most formidable operations, it is often beating with natural volume and force, not more than sixty or seventy times a minute. The pulse rarely becomes weaker or slower than natural under the influence of chloroform, except from considerable loss of blood, or where the patient is about to be sick. I have twice found the pulse as slow as 44 in the minute at the conclusion of an operation attended with great loss of blood. One of the cases was the removal of a large tumour of the labium pudendi, in a woman, aged forty-five, on the 28th of April, 1849, at King's College Hospital, by Mr. Fergusson. The pulse was, however, not small or weak, and there was no faintness. In a few minutes, the patient vomited, and the pulse immediately resumed its natural frequency.*

There is occasionally a feeble state of pulse with a feeling of faintness as the effects of the chloroform subside, and in two or three cases in which the patient was in a sitting posture, positive syncope occurred, which, however, was promptly removed by the horizontal position. The persons most liable to a feeling of faintness after chloroform, are those who are subject to syncope from slight causes.

* Since the above was written, I have met with an instance in which the pulse was only 40 in the minute, as the effects of the chloroform were subsiding. There was neither sickness nor loss of blood. The case was that of a gentleman in good general health, who inhaled chloroform whilst Mr. Brodhurst endeavoured to make forcible flexion of the femur on the pelvis. He woke without any unpleasant symptoms, and the pulse resumed its natural frequency.

Action of Chloroform on the Nervous System. Chloroform, when inhaled, immediately reaches every part of the nervous system through the circulation, and it acts on every part of that system from the first, as a careful observation of the symptoms proves. It does not, however, act equally on all parts of the nervous system, according to the quantity which is absorbed; some parts of that system have their functions entirely, or almost, suspended, whilst others are but little under the influence of the vapour, and it is owing to this fact that the most severe pain may be prevented without danger. M. Flourens made the following remarks respecting the action of sulphuric ether, and they apply equally well to the effects of chloroform, when it is inhaled gradually: "Under the action of ether, the nervous centres lose their powers in regular succession — first, the cerbral lobes lose theirs, viz., the intellect; next, the cerebellum loses its, viz., the power of regulating locomotion; thirdly, the spinal marrow loses the principle of sensitiveness and of motion; the medulla oblongata still retains its functions, and the animal continues to live: with loss of power in the medulla oblongata, life is lost."* I may add, that after the breathing has ceased, from the loss of power of the medulla oblongata, the ganglionic nerves still perform their functions, and the heart and intestines continue to move for a time, often with vigour.

Owing to the unequal effects of a given quantity of chloroform on different parts of the nervous centres, and owing to its acting also on the nerves, a variety of states may be met with during a surgical operation, some of which have often been thought curious, or anomalous. The most usual state of the patient during an operation, when chloroform is successfully administered, is one of perfect quietude, without any sign of consciousness or sensation. The patient under chloroform may, however, moan, or cry, or flinch, or show other symptoms which are usually thought indicative of pain, but without using any articulate language, or remembering anything of the operation afterwards. If his flinching or crying out has neither interfered with the surgeon, nor distressed the friends who may be present, a case of this kind may be considered satisfactory. A third condition of the patient under the influence of chloroform is that in which he talks, or laughs, or sings during the operation, his words having no reference to what is being done. If he is sufficiently quiet for the proceedings of the surgeon, the application of the chloroform must be considered successful, and this condition proves the absence of pain even more completely than that in which there is neither sign nor sound, except the breathing and pulsation of the heart and blood vessels. A fourth condition of the patient is that in which he is conscious, and can look on whilst the surgeon is performing a small operation, or the minor part of a large one, without feeling it, or whilst feeling it in a manner which is not painful. This condition, when it occurs, is the most satisfactory proof of the power of chloroform to prevent pain. It happens but rarely, however, and cannot be induced at will, and it is usually at the concluding part of an operation, during which the patient has been unconscious,

* Gazette des Hôpitaux, 20 Mars, 1847.

that this condition is met with. He wakes whilst there is still a vessel to tie, or a suture to be introduced, and does not feel it, owing, as was stated before, to some of the chloroform being detained in the extra vascular liquor sanguinis, whilst the brain has become almost free from the medicine. When the knife, or the needle, is felt without being painful, it is because the common sensibility, without being entirely abolished, is so much reduced, that what would otherwise cause acute pain only occasions an ordinary sensation.

A fifth state of the patient is met with when an insufficient quantity of chloroform has been administered or when its effects have been allowed to subside too soon. The patient may call out or complain in articulate words, such as "Oh, you are hurting me," and yet may assert afterwards that he had no pain, and knew nothing whatever of the operation. His own language at the time must, however, be held to decide that there was some pain, which made so slight an impression on the disordered mind as not to remain in the memory. Pain which is not remembered is of very little consequence, and probably is but slight in degree. It should not be judged of by the expression of the patient when he is but partially conscious, and using no self-control. Chloroform may, lastly, be administered so badly, that the patient simply falls asleep under the soothing influence of a very gentle dose, as he might sleep from an ordinary dose of opium, without being insensible, and, when the operation is commenced he wakes to full consciousness, and both feels pain and remembers it.

Patients, when insensible, sometimes moan or groan from the effects of the chloroform, and quite independently of the operation. The groaning or moaning comes on sometimes and even leaves off again, before the operation is commenced. When symptoms like those of pain are present during an operation, one may generally know whether they are the consequences of it, by observing whether or not they are connected with each cut of the knife. But even when a flinch or a groan follows each manipulation of the surgeon, it does not necessarily follow, provided the patient does not speak, that he is suffering pain. Some amount of consciousness is essential to the presence of pain, but many of the lower animals execute movements like those caused by pain, after the head is cut off, and when, of course, there can be no consciousness. Although the mind, under ordinary circumstances, is conscious of the attitude, gestures, and cries, which accompany pain, neither the intellect nor the will have any share in their production. On the contrary, they usually take place in spite of the efforts of the will to prevent them, and one may understand that, when consciousness and volition are suspended, the actions usually indicative of pain may, for want of control, be excited by slighter causes, and to a greater degree, than in the waking state.

It is certain that chloroform may prevent pain in two ways, either by rendering the mind unconscious of external impressions, or by removing the sensibility to these impressions, that is, by a true anæsthetic action, but usually, and always, when breathed in a full dose, it acts in both ways at once.

The patient sometimes supposes that he remembers all the particulars of the

operation, although he did not feel the pain, but on questioning him it is usually found that it is a dream which he remembers, and not the actual facts. It is extremely rare for a patient to assert that he has felt pain from the operation, when he has not felt it, but I have known this to happen once or twice, and a circumstance which was related to me by Mr. Robinson proves the possibility of it. He administered chloroform, or ether, to a lady, with the intention of extracting some teeth, but could not succeed in getting the mouth open, and the lady woke before anything had been done, and asserted that she had felt the operation. She inhaled again, and awoke, and repeated the same statement once or twice before the teeth were actually extracted.

I have heard it stated that patients have felt the pain of the operation, but have been unable to make any sign of feeling it. Such an occurrence may possibly take place when the chloroform is inhaled too slowly, or not in sufficient quantity; but I have not witnessed it, and it evidently cannot happen with a sufficient dose.

(*To be continued*)

Brit. J. Anaesth. (1954), **26**, 442.

A NEW ENDOBRONCHIAL TUBE FOR BRONCHO-PLEURAL FISTULA REPAIR

BY

W. N. VELLACOTT

The Royal Infirmary, Worcester

IN anaesthesia for the surgery of pulmonary tuberculosis, bronchial blocking appears to be the exceptional rather than the usual procedure. This is, no doubt, largely due to the much improved pre-operative treatment nowadays of patients with sputum. Moreover, there has not yet been published by those who practise bronchial blocking a convincing series to show that their cases have a lower collapse and spread rate than a series done under exactly similar conditions in the same hospital, but without the use of blockers. A decided advantage, of course, arises from doing a good deal of bronchial blocking, for when those cases come along which undoubtedly need it, one is well-practised, and little tempted to try and do without it.

Endobronchial toilet with a long suction tube and sucker is commonly used during and at the end of operation. Though this is useful, the practice is somewhat over-valued; bronchoscopy done after such a toilet will frequently show that more sputum needs removal. Whenever the state of the patient allows it, post-operative bronchoscopy is advisable, though this procedure is exhausting and may be dangerous. This is, however, the only reliable method of ensuring a reasonably clear bronchial tree.

The face-down position is used by only a comparatively small number of thoracic surgeons in this country. It serves the anaesthetist's purposes very well for upper lobectomies, but not so well for lower lobectomies where it invites spread to the middle lobe on the right side, and to a lesser extent to the upper lobe on the left side. It is in any case likely to remain restricted for use with those surgeons who prefer this position for surgical reasons.

Again, for surgical reasons only, thoracoplasty is still often done under regional anaesthesia. This is in spite of an anaesthetic mortality which as a result of accidental intravenous or intrathecal injection, or of an occasional overdose, is probably higher than under general anaesthesia. An operative field which is bloodless and quiet, with the lung moving away from the surgeon instead of towards him during inspiration, is an understandable attraction. Sputum cannot, however, be effectively cleared by a patient coughing under regional anaesthesia (Parry-Brown, 1948), and patients are usually discouraged from coughing during the operation.

There is at least one type of case where it is dangerous not to use a blocker, and yet difficult to find a suitable one. If a right upper lobectomy is followed by broncho-pleural fistula and empyema, a surgeon may decide to try and close the

fistula. This is usually done in the lateral position, so that the advantages of the face-down position are not available. One is therefore obliged to block off what is left of the right upper lobe bronchus to prevent the entry into the bronchial tree of pus and of blood which collects while the surgeon is getting down to the fistula. A Magill's or Thompson's blocker can of course be placed in the right main bronchus to occlude the right upper lobe bronchus, but this prevents the effectual use by a seriously ill patient of the whole of the right lung throughout the operation. The same disadvantage applies to the use of an endobronchial cuffed tube in the left main bronchus. There is usually too little of the stump of the right upper lobe bronchus left to allow the special short-cuffed Magill blocker to be placed in the bronchus itself. This procedure has been advocated for right upper lobectomy (Stephen, 1952). Its use would also be likely to enlarge the fistula.

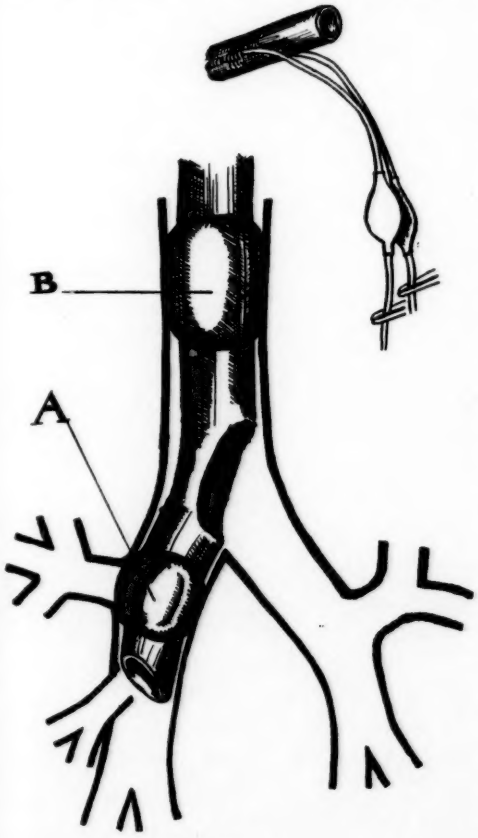

FIG. 1

The tube illustrated (fig. 1) offers a possible solution to the problem. It is a single-lumen latex tube, reinforced with spiral wire, and stiffened with an in-built malleable stilette. The purpose of the latter is to prevent a concertina effect when withdrawing the intubating bronchoscope with which the tube is used.

The tube has two inflatable cuffs. Cuff A is placed opposite the right upper lobe bronchus, occluding it; B remains in the trachea. Between the two cuffs there is a deeply cut, one-inch-long hole in the wall of the tube; this hole is directed towards the left main bronchus, and through it efficient exchange of gases takes place in the left lung. Very occasionally, the right upper lobe bronchus may be situated at too high a level in the right main bronchus for this procedure to be a safe one.

The tube cannot be used for operations on the left lung, as there is insufficient space for its distal end in the first part of the left lower lobe bronchus. The tube may, however, be used, if desired, for coping with cases of right upper lobectomy with excessive sputum. When blocking is considered necessary for this operation, I still prefer to try and place the short-cuffed Magill blocker in the right upper lobe bronchus. When this is done secre-

tions may be removed and not simply dammed back.

The endobronchial tube described probably has a limited use, but it may be found of value in the occasional difficult case. A similar reinforced latex tube has been designed for the left main bronchus during right pneumonectomy. It has an in-built stilette to prevent buckling, a single distal cuff, and no lateral lumen.

The tubes may be obtained from Talley Anaesthetic Equipment Ltd., 37a New Cavendish Street, London, W.1.

REFERENCES

Parry-Brown, A. I. (1948). *Thorax.*, **3**, 161.

Stephen, E. (1952). *Cur. Res. Anesth.*, **31**, 175.

BOOK REVIEW

Die Narkose. By Professor Dr. H. Killian and Professor H. Weese (late). Published by Georg Thieme Verlag. Stuttgart, 1954. Pp. 1003; 328 illustrations. D.M.170.

This massive textbook covers a vast field of physiology, pharmacology, physics and pathology in relation to anaesthesia. It also includes chapters on the clinical administration of anaesthetics. The authors — not anaesthetists themselves — have called on their clinical colleagues to describe the practical techniques of anaesthesia, and these sections will have to be amplified if the title of the book is to be justified. These latter chapters follow closely the clinical practice in the English speaking countries. They show the very great influence British anaesthesia in particular has had in raising the standard of anaesthesia in other countries. Reading the book, however, gives one the feeling that, in Germany at any rate, the clinical side of anaesthesia still takes second place to what has become known as the "scientific aspects" of the subject. No opportunity is lost of including tables, charts and graphs, whether these be of ranges of blood pressure at different ages, the mechanism of blood clotting, or function-localization in the brain. It might have been better to have placed the authorship in the hands of experienced clinical anaesthetists who could then have the appropriate sections written by expert surgeons, pharmacologists and others. Our own textbook edited by Frankis Evans could well serve as a model in this respect. These observations must not detract from the admiration excited by the enormous amount of material and the enormous labour that must have been spent in compiling it. Though some of the contents have only remote relevancy to clinical anaesthesia, the book as a whole will be of the greatest value for reference purposes. Research workers in particular will appreciate the very extensive lists of references. Whether a book like this will improve the standard of clinical anaesthesia in Germany, or raise the status of the anaesthetist sufficiently to attract men likely to be the future authors of textbooks, to take up anaesthesia as their life work is another matter.

W. W. Mushin

Brit. J. Anaesth. (1954), **26**, 445.

A SIMPLE T-PIECE

BY

P. D. KELSALL

Manchester Royal Infirmary

THE value of the T-piece principle in reducing the resistance an anaesthetic apparatus offers to respiration is well established. Unfortunately the commonly used Ayre's (1937) T-piece cannot be connected directly to the endotracheal tube. The angled connectors and pieces of rubber tubing which must be interposed markedly increase the resistance of the apparatus to respiration. To overcome this drawback a T-piece was designed, for use in adult patients, of a pattern which would make connections unnecessary. To this end the endotracheal tube was mounted directly on a side arm let into a wide-bore piece of metal tubing. As this T-piece was designed originally for neurosurgical work it was also necessary to provide for endotracheal suction and for a quick method of converting the open system into a semi-closed one should respiration become depressed and the patient require manual inflation of the lungs.

The connection consists of a metal tube $1\frac{1}{4}$ inches in length and 1 inch in external diameter. This tube is tapered on the inside at one end to take the smaller taper of the standard double-tapered endotracheal catheter mount. At the other end it is tapered on the outside to take a standard expiratory valve mount. From the mid-point of the side of this tube projects the attachment for the endotracheal tube and diametrically opposite this is a second small tube with a stopper attached to allow for endotracheal suction (fig. 1).

In use the endotracheal tube can be attached to the connection before intubation, with a stilette passed through the

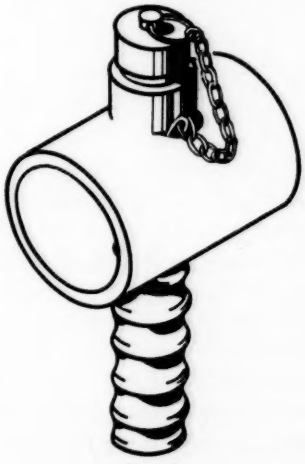

FIG. 1
The connection.

stoppered side tube if desired (fig. 2). Following intubation the connection and endotracheal tube are fixed in position with adhesive strapping. A double-tapered catheter mount, attached to a length of pressure tubing bringing gases from the anaesthetic machine, is inserted into the connection. A 3ft. 6in. length of standard wide-bore corrugated tube is attached on to the other end of the connection by means of a Heidbrink valve mount. If the distal end of the corrugated tube, with mount attached, is left open to the air the

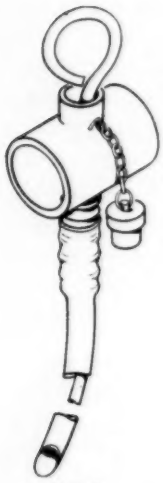

FIG. 2
The connection, with endotracheal tube and stilette in position, ready for intubation.

T-piece is complete (fig. 3; in the illustration a Heidbrink valve has also been left attached to the distal end of the corrugated tube). When, however, a short-acting muscle relaxant has been used for intubation or should respiration fail during anaesthesia it will be necessary to respire the patient by manual compression of a reservoir bag. This is accomplished by attaching a Heidbrink valve and a reservoir bag mounted on a valve mount to the distal end of the corrugated tube (fig. 4).

Apart from the T-piece connection all the equipment used, with the addition of the valve mount used on the reservoir bag, is standard equipment on the Boyle's machine. This connection has proved very simple in use and cases anaesthetized with its aid have been agreeably free from the venous oozing and raised intracranial tension associated with hypercarbia or any increased resistance to respiration.

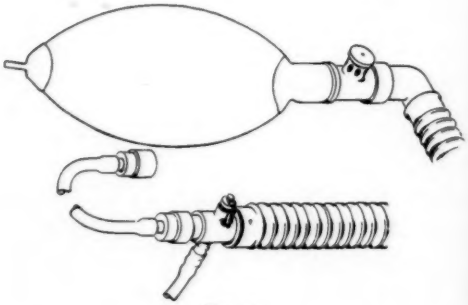

FIG. 4
The T-piece system converted into a semi-closed one when artificial respiration becomes necessary.

FIG. 3
The connection in use as a T-piece.

Although the connection was originally designed for neurosurgical work there is also scope for its use in such operations as mastectomy and thyroidectomy where the avoidance of venous oozing is of the utmost importance.

ACKNOWLEDGMENTS

I am indebted to Dr. H. J. Brennan for permission to publish and for his suggested modification of the original connection; to Dr. A. R. Hunter for his advice and guidance; and to the Department of Medical Illustration at the Manchester Royal Infirmary for the illustrations.

REFERENCE

Ayre, P. (1937). *Lancet*, **1**, 561.

CORRESPONDENCE

Sir,—Under the heading of "pethidine phlebitis", an expression originally coined by Wolfers (*Brit. J. Anaesth.*, **25**, 244), Argent and Dinnick (*Brit. J. Anaesth.*, **26**, 260) describe the urticarial or triple response of the overlying skin commonly seen following the injection of pethidine into a superficial vein. We would like to protest against the use of the term "pethidine phlebitis" as being both inaccurate and misleading.

There is evidence to show that the mechanism of this phenomenon is that, following the intravenous injection, pethidine diffuses freely through the vein wall to the skin where it releases histamine. This reaction is not peculiar to pethidine but may be produced by histamine and the histamine-liberating substances morphine and curare. There is also evidence that not only these four substances but also mepyramine and nux vomica are all able to diffuse through the walls of medium-sized veins (Finer and Partington, 1953).

There seems little reason to infer from these observations that the intravenous injection of pethidine causes or predisposes to venous spasm, "irritation", phlebitis or thrombosis. The release of small quantities of histamine in the skin is not attended by ill effects and it seems an unnecessary complication of the administration of pethidine to take steps to avoid it.

We submit, therefore, that the term "pethidine phlebitis" should be abandoned since it implies the existence of a sinister pathological state for which there is no evidence.

B. L. FINER
M. W. PARTINGTON
The London Hospital Medical College, Department of Physiology.

REFERENCE

Finer, B. L., and Partington, M. W. (1953). *Brit. Med. J.*, **1**, 431.

Sir,—We should like to comment on a statement made in your annotation on local vein reactions (*Brit. J. Anaesth.*, **26**, 283).

Your annotation stated that . . . "pethidine and thiopentone . . . when injected into the rubber tubing of the drip causes an immediate increase in the rate of the drip." This is undoubtedly so when the injected fluid raises the pressure sufficiently to clear a partially blocked needle, but at other times it is our experience that injection of either of these drugs is followed by an immediate slowing of the drip. Indeed such an injection may not infrequently stop an already poorly flowing transfusion. On the other hand the flow rate is ultimately increased when, for example, the resultant induction or deepening of anaesthesia abolishes the venous congestion in a "straining" patient, or reduces peripheral venous tone. Nevertheless, even under these conditions, we find that the increased flow is usually pre-

ceded by an immediate though transient slowing of the drip.

Finer and Partington, in their letter above, criticize the use of the term "phlebitis"—perhaps we strove too hard for a neat title—nevertheless chemical phlebitis is a recognized entity and, as your annotation says, may vary greatly in degree. We are not aware of any evidence that veins are permeable under normal conditions, and it does not seem unreasonable to deduce the presence of irritation and hence inflammation when pathological changes occur after contact with a foreign substance.

In conclusion we would point out that the "complication of administration", namely dilution of the drug, to which Finer and Partington object has the added advantage of facilitating accurate dosage as well as those discussed in our paper and your annotation.

D. E. ARGENT,
O. P. DINNICK,
*The Middlesex Hospital, London, W.*1

ROYAL SOCIETY OF MEDICINE

ANAESTHETIC SECTION PROGRAMME, 1954–55

The following meetings will take place at 5.30 p.m.

1954		
November 5:	Dr. Bernard Johnson	Presidential Address.
December 3:	Professor W. R. Spurrell	"Carbon Dioxide."
1955		
January 7:	Professor E. A. Pask	"The Maintenance of Respiration in Respiratory Paralysis."
February 4:	Dr. J. E. Hall	"Respiratory Physiology in Infants and Young Children."
March 4:	Dr. H. C. Churchill-Davidson	"Abnormal Responses to Muscle Relaxants" (with film).
April 1:	Dr. T. C. Gray, Dr. C. F. Scurr	"Induced Hypothermia."
May 6:	Short papers:	
	(1) Dr. C. Langton-Hewer	"The Complications of the Trendelenburg Position."
	(2) Dr. A. R. Hunter	"Problems of Anaesthesia in Patients with Artificial Pneumothorax."
	(3) Dr. J. Bullough	"The Reduction of Bleeding by T-piece Anaesthesia."

FACULTY NEWS

A SERIES of Pharmacology Lectures will be held at the College in Lincoln's Inn Fields, London, W.C.2, beginning on Monday, November 29, and ending on Friday, December 10, 1954. The programme is as follows:

Monday, November 29

4.30–5.30 Introduction. Toxic Reactions. Professor W. D. M. Paton

5.45–6.45 Drugs Acting on Autonomic Effector Organs I. Professor W. D. M. Paton

Tuesday, November 30

4.30–5.30 Drugs Acting on Autonomic Effector Organs II. Professor W. D. M. Paton

5.45–6.45 Drugs Acting on Neuromuscular Junction. Professor W. D. M. Paton

Wednesday, December 1

4.30–5.30 Drugs Acting on Ganglia. Professor W. D. M. Paton

5.45–6.45 Histamine and Antihistamines. Professor W. D. M. Paton

Thursday, December 2

4.30–5.30 Barbiturates and Hypnotics. Dr. J. W. Thompson

5.45–6.45 Analgesics. Professor W. D. M. Paton

Friday, December 3

4.30–5.30 General Anaesthetics. Professor W. D. M. Paton

5.45–6.45 Analeptics. Professor W. D. M. Paton

Monday, December 6

4.30–5.30 Local Anaesthetics. Dr. J. W. Thompson

5.45–6.45 Biochemistry of Nervous Tissue. Dr. J. E. Gardiner

Tuesday, December 7

4.30–5.30 Chemotherapy I. Professor W. D. M. Paton

5.45–6.45 Chemotherapy II. Professor W. D. M. Paton

Wednesday, December 8

4.30–5.30 Hormones I. Dr. J. W. Thompson

5.45–6.45 Hormones II. Dr. J. W. Thompson

Thursday, December 9

4.30–5.30 Drugs Acting on Heart and Circulation. Professor W. D. M. Paton

5.45–6.45 Drugs Acting on Respiration. Professor W. D. M. Paton

Friday, December 10

4.30–5.30 Drugs Acting on Kidney and Alimentary Tract. Professor W. D. M. Paton

5.45–6.45 Absorption, Distribution and Elimination of Drugs. Professor W. D. M. Paton

These lectures form part of the Basic Sciences Course, or if taken by themselves a fee of six guineas is charged. Individual lectures may be attended at a fee of ten shillings each. Application forms and admission cards may be obtained from Mr. W. F. Davis, Secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2 (Tel.: HOLborn 3474).

Educational Supplement
November 1954

THE CONTROL OF WATER AND ELECTROLYTE BALANCE AFTER SURGERY*

BY
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THE great majority of patients who undergo a surgical operation are able, within a very short while, to return to a normal intake of food and drink, so that, with regard to fluid balance, they present no problems which demand more than common sense in their management. However, in the minority of patients, particularly those submitted to major surgery on the alimentary tract, care is required if they are to be maintained in fluid and electrolyte balance in the days immediately following operation. The need for this care arises from two causes: first, because such patients are liable to develop complications such as paralytic ileus which can in themselves easily lead to severe electrolyte disturbance; secondly, because of the metabolic changes which follow surgery. This metabolic response to surgery occurs after all operations, indeed, after all forms of trauma. In general its magnitude varies in direct proportion to the magnitude of the trauma, with the result that, whilst it can be neglected after operations of average severity, an understanding and recognition of its effects is vital in the care of those submitted to major operations.

This post-operative response affects many of the metabolic processes of the body, indeed probably more than we are yet aware of, but its most important effects are on the handling by the body of water and electrolytes. Speaking in general terms these effects can be described as an impairment of the kidneys' normal ability to excrete from the body excess loads of water and salt. As a result, if too much fluid is given, it accumulates in the body, leading to salt and/or water retention. Such a retention is, of course, the end result of these metabolic changes but it is by observation of the details of such retentions that we derive our knowledge of the changes themselves. During the past few years my colleague Dr. Lewis and I have carried out a series of balance studies before and after operation which have enabled us to get a reasonably clear picture of these changes. Our results have been published elsewhere (Le Quesne and Lewis, 1953), and the description that follows will largely be based on our observations, which I should point out revealed little that was new. I shall not take up your time now with technical details, but before describing our results one or two points need emphasis. The essential basis of our observations was the

* Being the text of a lecture delivered at a Scientific Meeting of the Faculty of Anaesthetists of the Royal College of Surgeons of England, on June 19, 1954.

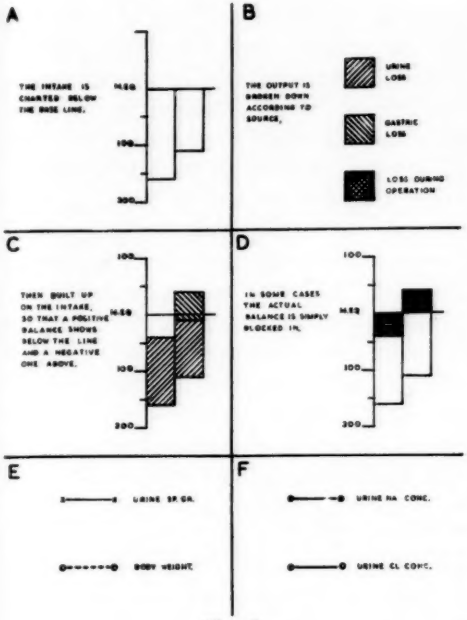


FIG. 1
Drawing showing the method of charting used in recording the balance studies.

use of a technique by which we could maintain a constant intake of water and electrolytes for several days before and after operation, the only variation being that after operation, when fluids were given intravenously, the patients received no protein and only 600 cals. per 24 hours. In most cases these patients were given 4 l. of water and 170 m.eq. of Na, that is 10 g. of salt, per 24 hours, and it must be emphasized that this intake was chosen not because it was considered optimal, but to make readily apparent any changes that might occur in water and salt excretion. The majority of the patients studied were undergoing subtotal gastrectomy for benign peptic ulcer. Balance studies were carried out in the usual way and in addition the patients were weighed daily: it is important to emphasize that on the calorie intake given after operation we would, under normal circumstances, expect these patients to lose weight at the rate of about $\frac{1}{2}$–1 lb. (0.2–0.5 kg.) per 24 hours, so that a stationary or rising weight in these circumstances is highly significant. The metabolic data obtained by these studies has been charted in the usual way, and for those unfamiliar with this type of charting figure 1 shows the principle of the method

The most immediately striking change found in the patients studied was the marked oliguria occurring in the first 24 hours after operation. This is illustrated by figure 2, which shows the urine output in six cases for three consecutive 24-hour periods, with the operation taking place at the start of the second of these periods.

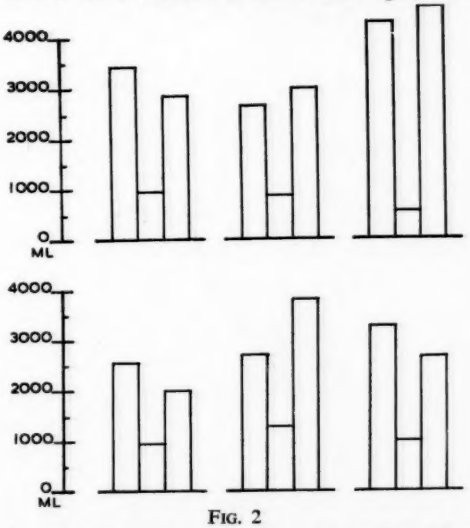


FIG. 2
Stick-graphs showing the 24-hour urine output, in six different patients, for three consecutive 24-hour periods. All six patients underwent subtotal gastrectomy at the start of the second 24-hour period. During each 24-hour period all these patients received 4 l. of fluid, and the diminished urine output following operation is clearly shown.

During each of these 24-hour periods all these patients received 4 l. of fluid, and the profound diminution in urine output following operation is clearly shown. With an intake of 4 l., this diminution in urine volume must lead to a retention of water in the body, and this is confirmed by the finding that all these patients showed a marked gain in weight during this 24-hour period, despite the fact that their calorie intake on this day was quite inadequate. Figure 3 records again the urine output from one of these patients, together with the body weight, which shows a clear-cut gain on the day of operation, followed on the next day, on which a diuresis occurred, by a similar fall. Also shown in this figure is the sodium balance, and it can be seen that, simultaneously with the water retention, on the day of operation there is a distinct retention of sodium, amounting to some 100 m.eq., most of which is excreted on the following day.

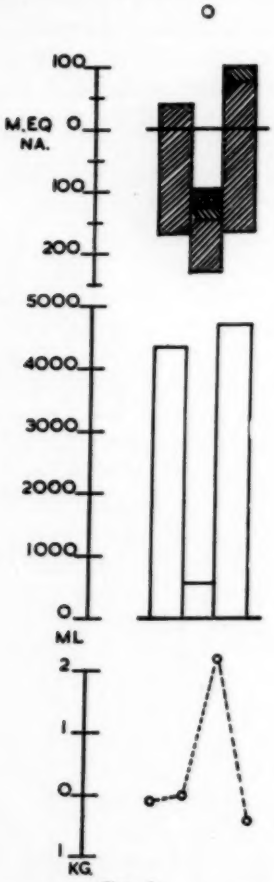


FIG. 3

Sodium balance, urine output and body weight for three consecutive 24-hour periods in a patient undergoing subtotal gastrectomy, and receiving 4 l. of water per 24 hours. The greatly diminished urine flow on the day of operation led to water retention, which is reflected by a weight rise of over 2 kg (4.4 lb.), despite an inadequate calorie intake. Simultaneous with the water retention, there is a considerable retention of sodium.

In view of the simultaneous occurrence of this sodium and water retention it would be easy to assume that the latter is dependent upon and caused by the former. But in fact this is not so, as it can be clearly shown that this water retention occurs whether or not salt (i.e. sodium) is given on that day. Figure 4 shows the results obtained in two cases who received no sodium on the day of operation, except for that contained in a pint of citrated blood. It can be seen that both were clearly in negative sodium balance on that day, yet both showed the weight gain of water retention, which must therefore be an independent, primary phenomenon. The figure also shows that in both these two cases there was a distinct rise in urine specific gravity on the day of operation, and this rise was one of the most characteristic features of the episode of primary water retention. In all the cases we observed, the diminution of urine flow on the day of operation was accompanied

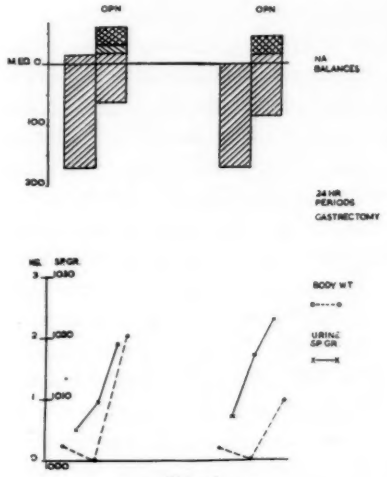


FIG. 4

Data from two cases who received no sodium on the day of operation, except for that in 500 ml. of citrated blood. Both patients were clearly in negative sodium balance during the 24 hours following operation, yet both showed a weight gain due to water retention. Note the rise in urine specific gravity during the 24 hours after operation.

by a marked rise in the urine specific gravity and by a similar rise in the urinary concentration of sodium and chloride, all three of which usually fell to pre-operative levels during the subsequent 24-hour period. These changes in urine composition are well seen in figure 5, which shows the relevant data from the case previously illustrated.

Now these observations based on the analysis of 24-hour pooled specimens of urine necessarily give but a crude idea of the nature and duration of a change such as this. However, more detailed information can be obtained if studies are made on 4-hourly urine specimens obtained from patients requiring an indwelling urethral catheter after operation. These studies, of which figure 6 is a typical example, show that coincident with the start of the operation there is an immediate fall in the rate of urine flow, together with a rise in urine specific gravity and chloride concentration. After an operation of moderate severity, like a sigmoid colectomy, these changes last some 24–36 hours, after which there is a diuresis, and return of specific gravity to normal levels. As has already been shown, this change is independent of the intake of salt, and under

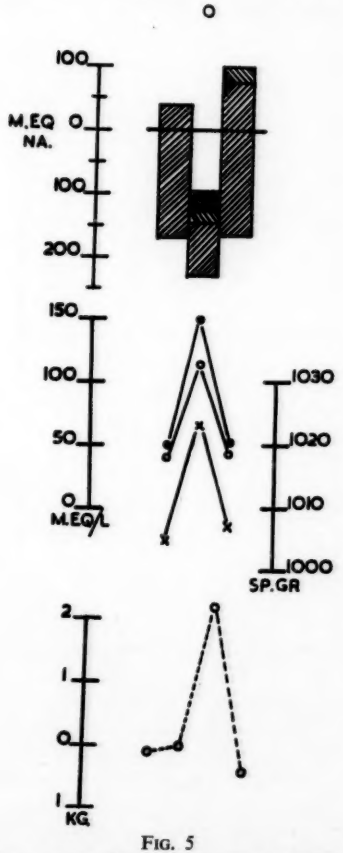
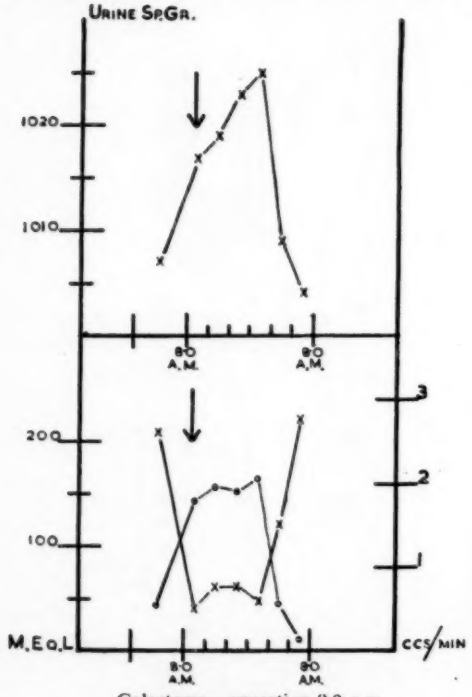


FIG. 5

Further data from the case illustrated in figure 3. On the day of operation there is a marked rise in the specific gravity and sodium and chloride concentrations of the urine, with all three falling to pre-operative levels on the following day.

suitable circumstances can lead to considerable retention of water.

This alteration in the excretion of water, this episode which we have called "primary water retention", is but one facet, certainly a very important one, but only one facet of the post-operative metabolic response. The tendency to retain sodium on the day of operation has already been mentioned and there is a further, more prolonged, period of interference with sodium excretion, as shown in figure 7. The retention of sodium on the day of operation is clearly shown, and in all our cases there was a clear-cut retention on this day. However, the predominant phenomenon during this 24-hour period appears to be the episode of "primary water retention" just described, and it is the characteristics of this latter that we see in the urine, with the paradoxical result that this incident of sodium retention is accompanied by a high urine sodium concentration, though low sodium excretion. But on the second, third, and fourth days after operation there is a further period of diminished urinary excretion of sodium, leading to sodium retention and this time accompanied by a lowered concentration of sodium in the urine: at the same time there is a further retention of water, as is shown by the further rise in body weight despite the continuing inadequate calorie intake. This second, more prolonged episode of simultaneous water and sodium retention differs fundamentally from the independent episodes of water and salt retention occurring on the day of operation, in that during this latter period the two are integral parts of one phenomenon, the water retention being caused by the salt retention. Figure 8 shows the results obtained in one of the cases who received no salt after operation, except for that in a bottle of blood during the operation. In this case, in negative sodium balance for 4 days after operation, a second rise in weight did not occur until eventually salt was given, showing conclusively that during the later episode of retention the water retention is a secondary event, dependent upon and integrated



Colectomy—operation 9.0 a.m.
o——o Urine cl. concentration.
x——x Min. vol. urine.

FIG. 6

Results obtained by examination of 4-hourly urine specimens from an indwelling, urethral catheter, in a patient undergoing sigmoid colectomy. Operation (marked by the arrow) is followed by a profound fall in the rate of urine flow, which lasts for 20 hours. This diminution in urine flow is accompanied by a simultaneous rise in urinary specific gravity and chloride concentration.

with the episode of late sodium retention.

In further contrast to the events on the day of operation itself this phenomenon of late sodium retention is distinctly variable, in its magnitude, in its duration, which is largely dependent on the severity of the operation, and in the time of its onset. In many of our cases late sodium

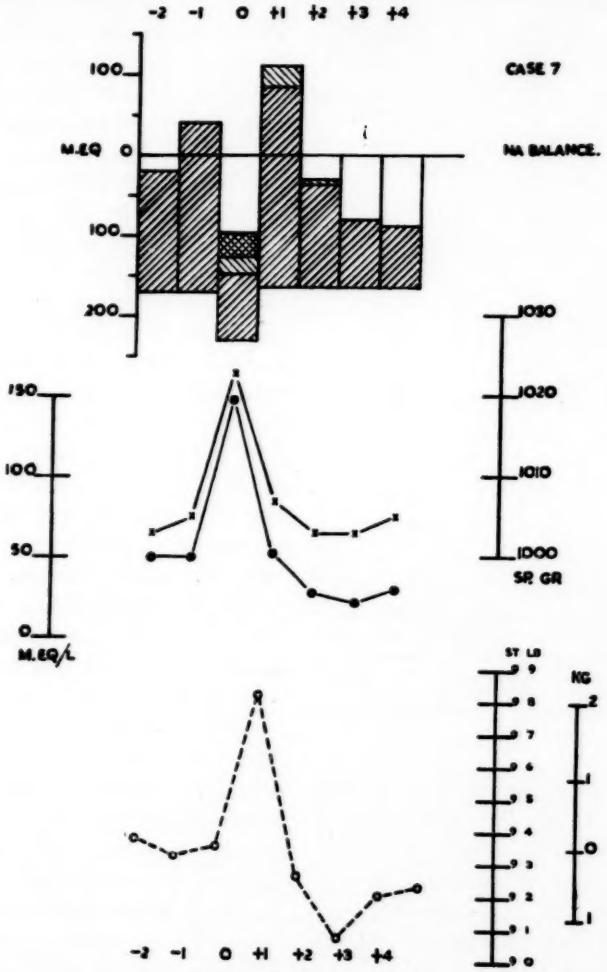


FIG. 7

Balance data from a case undergoing subtotal gastrectomy. On the day of operation there are simultaneous but separable episodes of salt (sodium) and water retention, the effects of the latter being reflected in the weight gain and urine changes. On the second, third, and fourth days after operation there is a further, more prolonged, period of salt (sodium) and water retention, this time accompanied by a lowered urine sodium concentration.

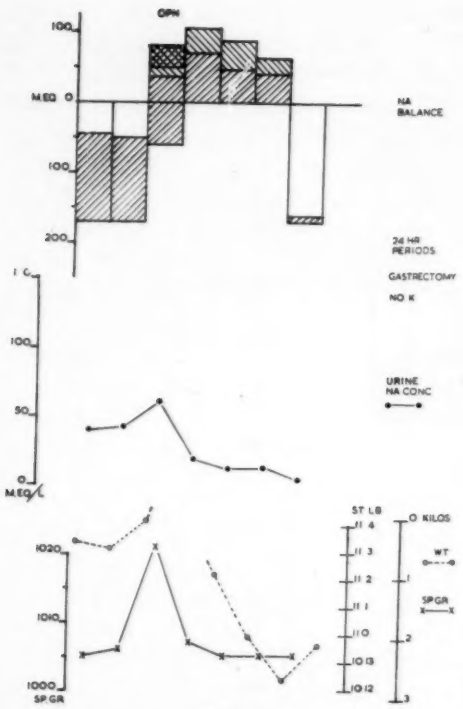


FIG. 8

Data from a case receiving no sodium after operation, except for that in 500 ml. of citrated blood. The body weight was not recorded on the morning after surgery, but thereafter there was a steady fall until sodium (salt) was given, showing that during this second period the water retention is dependent upon salt retention.

retention developed earlier than in the case illustrated, with the result that it tended to merge to a greater or lesser degree with the sodium retention on the day of operation. As is shown in figure 9 this led to varying patterns of sodium retention, which are reflected not only in the sodium balances but also in the urine sodium concentration figures and in the weight curves. It is to be noted that in many cases this leads to a continuous period of salt and water retention lasting for 4–5 days after surgery. During the first 24–36 hours after operation the interference with the excretion of water is the dominant feature, but thereafter the equally important interference with sodium excretion becomes prominent, causing a combined retention of sodium and water. It is the fusion of these phenomena which gives rise to the complex disturbance of fluid balance after operation and to the varying patterns of response which may occur.

So far the only aspects of the post-operative metabolic disturbance to be considered have been the changes in the handling of water and salt, but mention must be made of the increased urinary loss of nitrogen and potassium which occur after operation. For up to 3 days after operation there is a markedly increased loss of nitrogen in the urine: even if an adequate intake of protein is given during these days this loss cannot be reversed and necessarily leads to a negative nitrogen balance. Similarly, during this time there is an increased urinary excretion of potassium, which is relatively in excess of the nitrogen excretion and so must be indicative of a mobilization of intracellular potassium. Again, this cannot be prevented by giving potassium during these days, and this increased urinary loss of potassium during the 24–48 hours immediately following surgery is one of the most important causes of post-operative potassium depletion.

Turning to the aetiology of these metabolic changes after operation it is now apparent that more than one mechanism is at work. It can be said straight away that the changes occurring after operation are not the same as those found in starva-

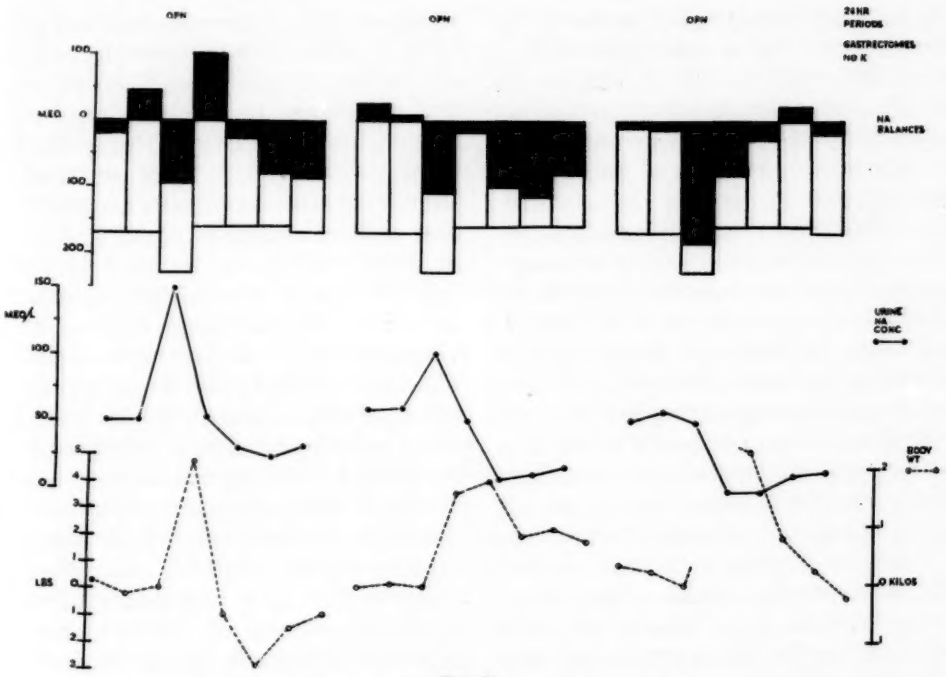


FIG. 9

Data from three cases undergoing subtotal gastrectomy (balances blocked in), showing the varying patterns of sodium retention. In the left-hand case the second, prolonged period of sodium retention is clearly separated from that on the day of operation: in the middle case, whilst not clearly separated, the two episodes are still distinct, but in the third case they have completely coalesced. This variation in time of onset of the late sodium retention is reflected in the curves of urinary sodium concentration, which show their maximum fall on the third, second, and first days after operation respectively. The weight curves also reflect the timing of the later retention.

tion, so that they cannot be explained on the simple grounds of an inadequate calorie and protein intake. It is now equally clear that after operation there is an increased liberation of adrenocortical hormones, which is in great part responsible for these changes (Moore and Ball, 1952). The increased excretion of nitrogen and potassium, the retention of sodium and other changes such as the fall in the eosinophil count are all highly characteristic of an adrenocortical release, and there is overwhelming evidence that they are in fact due to this cause. However, two distinct difficulties arise in accepting the adrenal cortex as the sole cause of the whole post-operative disturbance. First, the sodium retention appears to occur in two distinct waves: there are a number of possible explanations for this, of which the most likely seems to be that the retention on the day of operation is at least in part due to renal haemo-dynamic changes. Secondly, and of far more importance, is the fact that the features of primary water retention in no way resemble the action of

any known adrenocortical hormone: but these features, that is a diminished rate of urine flow with a urine of high specific gravity and chloride concentration, are precisely those produced by secretion of the antidiuretic hormone of the posterior pituitary gland. Recently Dr. Lewis and his colleague Dr. Eisen (Eisen and Lewis, 1954) have shown by bio-assay, in alcohol-anaesthetized rats, that the urine during the first 24 hours after operation contains a strongly antidiuretic substance, which, whilst not definitely identified as A.D.H., has properties which strongly support this hypothesis, and we believe that the interference with water excretion immediately after operation is in fact due to this hormone. There is no evidence that the usual stimulus of hypertonicity is the cause of the post-operative release of antidiuretic hormone, but it is known that pain, emotion, trauma and drugs such as pethidine and morphia can cause such a release and it is probable that a summation of these stimuli accounts for the prolonged secretion occurring after operation. To sum up then, we may say that whilst the adrenal cortex is responsible for many of the metabolic changes after operation, it appears probable that the antidiuretic hormone also plays a significant part, and it may well be that other factors contribute in producing the final, complex pattern of disturbance that has been outlined.

Whilst the exact details of their manifestations and aetiology are complicated and still partly obscure, the clinical significance of these post-operative metabolic changes is clear. In normal circumstances the kidneys are remarkably flexible in action and are capable of excreting from the body, in a short time, excess loads of water and salt. After operation this flexibility is replaced by a temporary rigidity of function, so that excess loads of water and salt cannot be eliminated and must accumulate in the body. I have already mentioned that in the cases we observed the intake was deliberately arranged so that definite retention of salt and water occurred, and I have described the metabolic changes in terms of these episodes of retention. But, of course, such retention after operation is not inevitable. What are inevitable are the metabolic changes themselves, which necessarily follow all operations, and whether or not a retention of salt or water occurs depends entirely on the intake of these substances. Not only is a retention of salt or water after operation not inevitable, but all the evidence suggests that it is undesirable. If only moderate excesses of salt or water are retained little harm can occur, but it is quite easily possible during the first few days after operation to produce serious, even fatal, clinical syndromes by overloading with either salt or water. As has already been described, the impairment of salt excretion lasts for 3 or 4 days after an operation of average severity, and throughout the whole of this time there is a danger of overloading. If such overloading is gross, a well recognized clinical picture develops with oedema formation, waterlogging of the lung bases and even a rise in the jugular venous pressure, but lesser degrees of overloading with salt can equally cause serious trouble owing to oedema formation in wounds, in intestinal suture lines and at the lung bases, all of which can lead to highly undesirable complications. This danger of giving too much salt (saline) has been recognized for many

years, but the risks of excessive administration of water are less well appreciated. During the first 36 hours after operation, when its excretion is impaired, water, usually given intravenously in the form of 5 per cent dextrose, is just as potentially dangerous as saline, and during this period it is quite easily possible to produce acute water intoxication (Le Quesne, 1954). As described recently by Wynn and Rob (1954) more chronic states of water intoxication can occur later in the post-operative period for reasons which are as yet obscure, but undoubtedly the main danger of precipitating this condition occurs during the first 36 hours after operation. Acute water intoxication presents usually with extreme restlessness, disorientation and behaviour disturbances, going on to convulsions, coma and death. In these cases examination of the fluid balance chart will always show a gross excess of intake over output, and as would be expected there is hypotonicity, with a marked fall in the plasma electrolyte concentrations. Gross manifestations of water retention such as this are not common, but, just as with salt, lesser degrees of water retention can be harmful, and probably much post-operative nausea and vomiting is in great part due to mild water overloading.

The problem, then, in the first few days after operation is to provide a basic intake of water and electrolytes which whilst not so small as to cause any depletion, is yet not so great as to allow of any sizeable retention. In those patients who can take fluids by mouth within a few hours of operation, the problem scarcely arises, because their own tastes are usually a safe and sufficient guide. But it cannot be stressed too strongly that no route of administration is immune to the dangers of overloading, and in this respect fluids given per rectum are just as potentially dangerous as those given intravenously. But for obvious reasons the problem demands most serious consideration when fluids are being given intravenously. Bearing in mind that the whole post-operative metabolic response is made up of several separable phenomena, it would be possible to design an intake which varied to meet the changing dangers, but experience shows that this is unnecessarily complicated and only leads to confusion. As will be explained, the markedly impaired ability to excrete water during the first 24–36 hours after operation imposes special restrictions, but otherwise a uniform intake can be given.

Whilst in no way minimizing the dangers of overloading, it should be borne in mind that during the first few days after operation, even in uncomplicated cases, there are likely to be increased losses from the body, both from increase in the cutaneous loss and, in abdominal cases, as a result of some pooling in the intestines from mild, transient ileus. Accordingly, if the basic intake is fixed too low, constant additions may be necessary, thus destroying the essential value of a basic intake which should in itself suffice except in complicated cases. Whilst undoubtedly the main danger after operation is that of overloading, we should not allow this to make us fall over backwards and give too little.

Considering first the water intake, there seems no reason to believe that 2.5–3.0 l. per 24 hours is too much, after the period of so-called "primary water retention" has passed: this allows an adequate margin for the cutaneous loss, and at the same

time provides a generous urine output. However, during the period of primary water retention, that is for the first 24–36 hours, such an intake is undoubtedly too high and will lead to retention, so that during this time the water intake should be restricted to 2 l. per 24 hours. Experiences show it to be safe to increase the intake from 2 l. to 3 l. after 24 hours, and for a while we invariably did this. However, bearing in mind that one of the most characteristic features of primary water retention is a raised urinary specific gravity, we now use this as our guide, and directly the gravity falls below 1010 increase the intake up to 3 l. per 24 hours. In practice there is probably little to choose between these two methods: the former is undoubtedly the simpler and the latter the more elegant, but the important point is that the intake should not exceed 2 l. in the first 24 hours, but thereafter it can be increased up to 3 l. per 24 hours.

Turning to the salt intake, the amount contained in 500 ml. of normal saline, that is 4.5 g. of NaCl or 80 m.eq., constitutes a satisfactory daily intake. Whilst providing a slight margin for any surplus losses there is no reason to believe that this amount can cause any dangerous retention, and it is, in addition, practically a most convenient amount to administer. Considering the first 24 hours after operation, the intake of 2 l. of water and 4.5 g. NaCl is provided by giving three ½-l. bottles of 5 per cent. glucose and one of normal saline, and thereafter this can be increased by the addition of two more bottles of 5 per cent glucose, bringing the total intake to 3 l. per day, that is three of the standard ½-l. bottles per 12 hours. It is to be noted that in many hospitals the standard bottles of intravenous fluids contain not ½ l. but one pint, but as the difference between these two is only some 60 ml. it can be neglected. If it is preferred, the salt can be given as 1/5 or 1/3 N saline, but it must be emphasized that such a practice in itself in no way minimizes the risks of excessive administration, and in my experience is more liable to lead to confusion.

Whilst this intake is perfectly adequate in most cases, there is much to be said in favour of adding to it some potassium. Perhaps the most important factor in the development of post-operative potassium deficiency is the increased urinary loss after operation occurring in the absence of a potassium intake. It seems illogical to let this deficit go unchecked and then later in some cases have to treat an established deficiency. There is no certain evidence as to what constitutes the optimal and entirely safe potassium intake in these circumstances, but we have been giving 6g. KCl, that is 80 m.eq. K, per 24 hours without any untoward effects. Owing to the oliguria immediately following operation, potassium should not be given during this period, and it has been our practice to add the potassium at the time the water intake is increased from 2 l. to 3 l. per 24 hours. Rather than give the patient some normal saline followed by a potassium chloride solution, it is simpler to give them together as a potassium-saline mixture. We have been using a mixture containing 2.25 g. NaCl and 3.0 g. KCl in a litre of 5 per cent dextrose, giving a potassium solution of 40 m.eq. per litre, which is the maximum strength which should be used for intravenous administration. Using this mixture, the daily ration of 3 litres of

water, 4.5 g. of salt and 6.0 g. of KCl is provided quite simply by giving each 12 hours two ½-l. bottles of the mixture and one ½-l. bottle of dextrose, except, as already stated, during the first 24 hours when the potassium is omitted and the water restricted to 2 litres. During the past two years in the Department of Surgical Studies we have now used this basic intake as a routine, and found it to give excellent results in a wide variety of cases. Experience shows that not only is it safe, but that it in fact constitutes a satisfactory basic intake which rarely needs alteration; we have found no complications from the routine use of potassium, except for occasional discomfort, and in our experience this practice virtually abolishes the occurrence of post-operative hypokalaemia. In order to assess its exact results, balance studies have been carried out on some of these patients, and these show that on this intake no significant retention of salt or water takes place, and that the potassium intake likewise does not give rise to danger of intoxication (see figs. 10 and 11).

Although this intake just described does not allow any significant retention to take place, it must be remembered that the post-operative metabolic changes themselves still take place and will lead to certain alterations in the urine which must be recognized for what they are if serious mistakes are to be avoided. For the first 24–36 hours after operation there will necessarily be a diminished urine output of raised specific gravity: as explained, this is simply a manifestation of the kidneys' temporary inability to excrete water normally and must not be interpreted as being significant, as it usually is, of water shortage, and so as an indication to increase the water intake. Similarly, during the second to fifth days after operation the urine chloride concentration will be below normal, but again this is simply a manifestation of impaired ability to excrete salt and must not be taken *per se* as an indication to increase the salt intake. The intake described is a fully adequate basic intake and should only be added to if there is definite evidence of abnormal losses, as by vomiting or intestinal suction, and, indeed, in any case of doubt it is probably wiser to give less rather than more fluid.

However, this intake is only designed as a basic intake to replace losses by normal routes, and further problems are raised if abnormal losses do occur. By far the commonest cause of such losses after operation is the development of in-

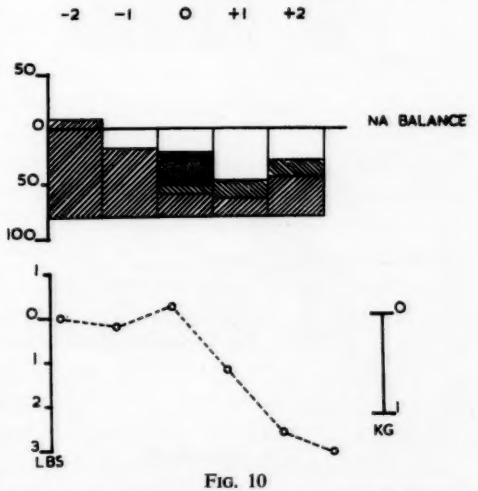


FIG. 10

Sodium balance and weight curve from a patient undergoing gastrectomy, who received the standard intake recommended in the text. The steady fall in weight after operation shows that no significant water retention occurs and the sodium retention is also insignificant.

testinal obstruction, paralytic ileus, or some form of fistula, such as a biliary, duodenal, or ileal fistula. All these conditions lead to loss from the body of intestinal juices, and a consideration of two simple facts concerning these fluids yields the key to the solution of the problem of the management of these losses. The normal volume of intestinal juices secreted in 24 hours amounts in all to over 8 l. that is more than twice the normal plasma volume (fig. 12). When it is remembered that in cases such as intestinal obstruction an increased quantity of intestinal fluids may be secreted, it is at once apparent that very large quantities of fluid can be lost rapidly from the alimentary tract and its associated glands, emphasizing the paramount importance of accurate measurement of these losses so that accurate, volume-for-volume replacement can be carried out. Figure 13 shows the composition of these juices and it will be seen that whilst their exact constituents vary, all of these fluids are essentially isotonic, so that they must be replaced not with glucose but with saline. The cardinal rule, then, in the treatment of observed, abnormal losses is first their accurate measurement, and then exact replacement, volume-for-volume with normal saline, this fluid being given in addition to the basic intake.

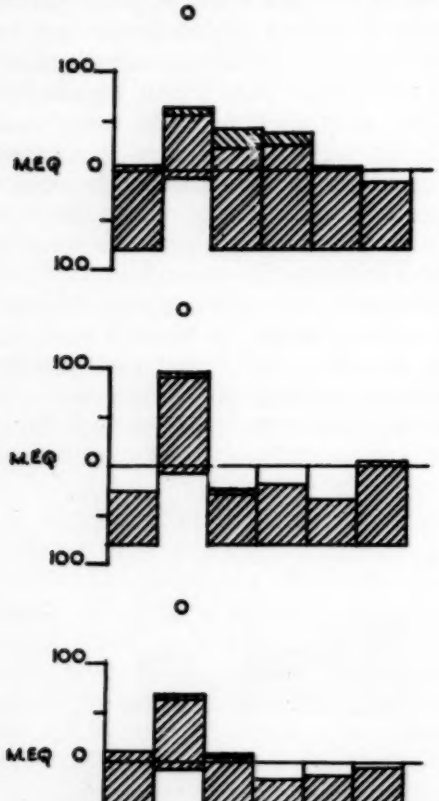


FIG. 11

Potassium balances from three patients undergoing gastrectomy who received the standard intake recommended in the text. As would be expected all three were clearly in negative balance on the day of operation itself. In none of the cases does the balance show any dangerous retention with this intake.

Source	*Volume*
Saliva	1500 ml.
Gastric Secretion	2500 ml.
Bile	500 ml.
Pancreatic Juice	700 ml.
Secretion of Intestinal Mucosa	3000 ml.
Total	8200 ml.
Normal Plasma Volume	3500 ml.

FIG. 12.
The normal volume of intestinal juices secreted per 24 hours by an adult (from Gamble, 1950).

Three obvious criticisms of this simple scheme come to mind, and must be considered, first, that the losses consist, not

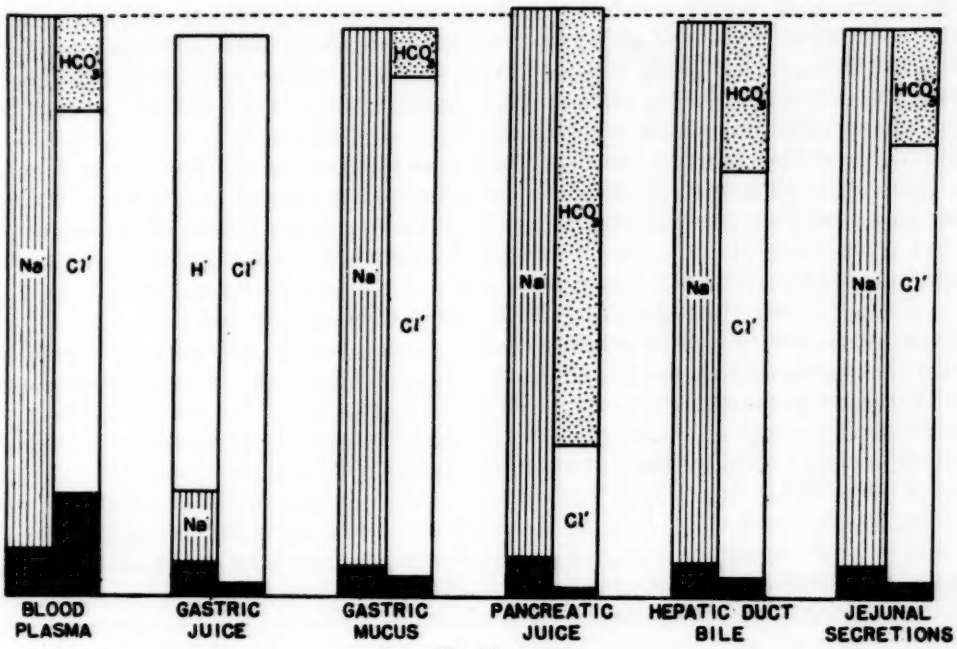


FIG. 13

Stick-graphs showing the composition of the various intestinal secretions (from Gamble, 1950).

of normal saline, but of fluids containing varying quantities of sodium and chloride; secondly, that in most cases the fluid lost is to some extent diluted by ingested water and therefore is not isotonic but somewhat hypotonic; and thirdly, that the fluids lost contain potassium. In the great majority of cases the fact that the fluids lost contain an excess of either sodium or chloride, and so cause a tendency to either acidosis or alkalosis can be neglected; if the losses are replaced by normal saline the kidneys will excrete whichever ion is in excess, and it is only rarely necessary to use special solutions such as sodium lactate or ammonium chloride to correct an acid-base disturbance. However, the kidneys can perform this function of adjusting the acid-base balance only if they are given adequate water in which to excrete the ions in excess, and this emphasizes the necessity both of replacing the losses accurately and of maintaining carefully the basic intake. If this is not done and only small quantities of urine are formed, then indeed acid-base disturbances may develop. As regards the tonicity of the fluids lost, there is no doubt that in many cases they are definitely hypotonic, but in my experience this is of no significance unless the losses are large, when it becomes necessary to take this into account and to modify not the quantity but the type of fluid given. A useful working rule is that if in any 24-hour period the losses exceed 2 l., then the fifth $\frac{1}{2}$-l. bottle of

replacement fluid should consist of glucose not saline, so as to prevent giving excessive quantities of salt. Turning to the point about potassium, most of the intestinal fluids contain potassium in a concentration two or three times greater than that of plasma, so that losses of these fluids can lead to a deficit of potassium, particularly when these losses are superimposed upon the increased urinary loss of potassium which occurs after operation. As a result, when abnormal losses are large or long continued, it is wise to add potassium salts to the replacement fluid, unless the basic intake contains this ion. Again, a useful working rule is that potassium should be added if the losses in any given 24-hour period exceed 2 l. or if the losses continue for more than 48 hours. In giving such potassium the usual precautions governing the intravenous administration of this ion must, of course, be observed. These may be summarized as follows: the total daily intake should not exceed 80 m.eq.K, that is the amount contained in 6 g. KCl, it should not be given in a concentration in excess of 40 m.eq./l., or at a rate in excess of 20 m.eq./hr. Further, potassium should not be given intravenously unless there is a reasonable urine output and good kidney function, and until considerable experience in its use has been obtained, it is wise to ascertain the serum K concentration before starting administration, and at daily intervals whilst it is being given. To sum up these considerations, we may say that observed losses must be replaced volume-for-volume with normal saline, except when these are severe, when the type not the quantity of the replacement fluid must be altered.

Whilst the replacement of abnormal losses is probably the most frequent problem to be faced after operation, another not uncommon situation demanding equally careful management is provided by the patient with a very low or even absent urine output. Provided the patient was not depleted of salt or water before operation, there are four likely causes of this happening and it is important that in any given case the cause should be accurately diagnosed.

Some months ago I was asked to see a woman who, 28 hours previously, had undergone a Caesarean section. Since the operation she had passed no urine and a provisional diagnosis had been made of acute tubular necrosis. Examination showed an apparently healthy young woman and inquiry showed that in the time since operation her intake had been only 200 ml., and a satisfactory urine flow was rapidly restored by giving a suitable intake. An inadequate intake is the most obvious cause of oliguria after operation and in such cases a careful examination of the intake chart over the preceding 12–24 hours will enable the diagnosis to be made. The obvious treatment in such cases is to increase the fluid intake, and if this results in an adequate urine output the diagnosis is confirmed. However, in many cases the intake has been quite adequate and then other causes must be considered. The most likely reason in these circumstances for an absent or inadequate urine output is that the patient has developed abnormal losses which have not been replaced, and again this diagnosis can usually be reached by a simple clinical examination of the patient, and an inquiry into his progress over the preceding 12–24 hours. If such an inquiry does reveal that

abnormal losses have occurred, then these should be replaced in the manner just described, and once again a return of urine flow will confirm the diagnosis The problem becomes more difficult when inquiry shows that not only has the intake been adequate, but also that there have been no abnormal losses. This situation usually arises during the first one or two days after operation, and the first possibility to be considered is that the oliguria is but an extreme manifestation of the normal post-operative metabolic response, and that the impairment of the kidney's ability to excrete water is unusually severe or prolonged. In such cases clinical examination will probably show nothing abnormal, unless sufficient retention has occurred to cause the early signs of acute water intoxication; examination of the urine will show a persistently high specific gravity, probably above 1020, with a high chloride concentration but no albumen or red cells. Once this diagnosis has been made no attempt must be made to force the urine output by increasing the intake, as this can only lead to water retention and possibly intoxication: instead, the intake should be restricted to about 1 l. per 24 hours, sufficient to cover the pulmonary and cutaneous loss, until a diuresis shows that the episode of primary water retention has passed, and a normal intake can again be given.

There remains for consideration the fourth and last common cause of oliguria after operation, namely acute tubular necrosis. This condition is generally considered to cause anuria but it is important to remember that in many cases it may only lead to severe oliguria. In these cases inquiry will probably show that the intake has been adequate and that there have been no abnormal losses, but of greater importance, it will in nearly every case reveal the aetiological incident, which is usually a profound fall in blood pressure during or after operation, or may unhappily be a mis-matched transfusion. The diagnosis will certainly be suggested by a history such as this, and is confirmed by finding in the urine albumen, casts, red cells or blood pigment. The treatment of this serious condition is beyond the scope of this lecture, but it must be emphasized that again no attempt should be made to force a urine flow by increasing the intake. Instead, the intake should immediately be restricted to 1000 ml. per 24 hours and treatment along the lines of the Bull régime instituted.

It is not for me to remind this audience that after operation many other problems can arise in respect of water and electrolyte balance, in particular, the problem of potassium deficiency in patients whose losses have otherwise been adequately replaced. But without a doubt these two problems, namely those of the management of abnormal losses and of an unexpectedly low urine output, constitute the two commonest and most important disturbances of fluid balance which occur in the post-operative period. I hope I have been able to show that in essence the treatment of both these conditions is reasonably simple, though actually at the bedside the circumstances of the case may make their successful control quite difficult, owing to the nature of the patient's original disease, or to severe shock or other complications and distractions. And always their control is rendered somewhat complex in that it must be carried out against the back-

ground of the metabolic changes occurring after surgery.

In describing the methods by which these two disturbances may be treated, quite deliberately little mention has been made of biochemical investigations of the blood or urine, and emphasis has been laid on simple clinical observations augmented by careful measurement of intake and output. Experience shows that these simple measures, applied with discretion, can be relied upon, and indeed they must form the main supports in treatment during the first few days after operation. Normally when a deficit of water or salt is being replaced, these measures can be checked by simple biochemical tests on the blood and especially the urine. But during the post-operative period the constituents of the urine are powerfully affected by the inevitable post-operative metabolic changes and so will be of little or no guide in the correction of other disturbances. Thus, normally the finding of the urine specific gravity to be above 1020 is, in the absence of glycosuria, practically diagnostic of water deficiency: but in the first 24 hours the urine specific gravity is always, as emphasized previously, at about this level, so that in these circumstances it gives us no guide as to whether the patient is short of water or has an excess in his body. Similarly the urine chloride figure will be of little help for the first three or four days after surgery. This point is well illustrated by figure 14 showing the sodium balance of a patient who developed severe paralytic ileus after a gut resection for strangulated hernia. This ileus led to large losses of fluid by suction from an indwelling gastric tube and these were replaced much in the way just described. It can be seen that on the third and fourth days the urine chloride concentration was nearly zero: at first glance this suggests that the patient was short of salt and that the replacement was inadequate; but in fact we can see that the replacement was excessive and that whilst the urine chloride concentration was at its lowest the patient was in strongly positive sodium balance. In other words,

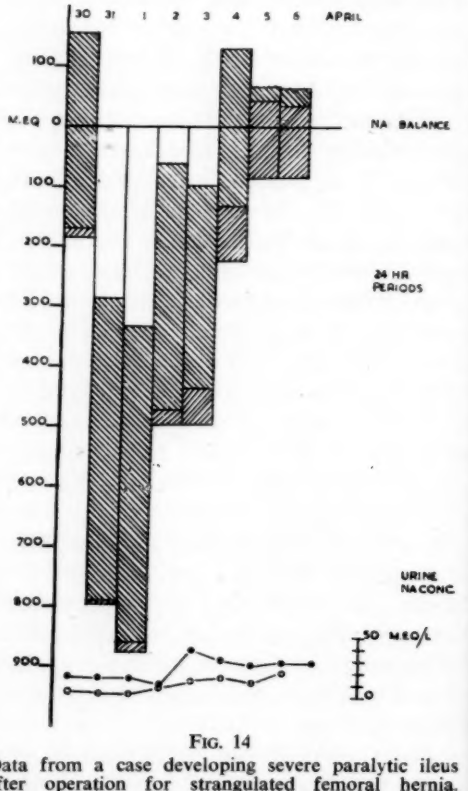


FIG. 14

Data from a case developing severe paralytic ileus after operation for strangulated femoral hernia. Operation took place on the day before the balance studies were started. Losses were replaced on a volume-for-volume basis: as the basic intake in this case was too high, this led to excessive administration of salt with considerable retention. Note that on the day of maximum retention the urine chloride concentration was nearly zero. In these circumstances this is not indicative of a shortage of salt, but is a manifestation of the metabolic disturbance following surgery.

in these circumstances the urine chloride concentration is a reflection not of the patient's state of salt balance, but of the impairment of the kidneys' ability to excrete salt which always occurs after operation.

This temporary restriction in the methods available for the control of water and electrolyte disturbances emphasizes the necessity for two steps which together form the essential basis of the successful management of fluid problems after operation. First, if at all possible, any pre-existing electrolyte disturbance must be corrected before operation. In any circumstances the replacement of pre-existing losses is always more difficult than that of observed losses, and the problem becomes doubly difficult in the post-operative period when some of the essential guides to this process are rendered valueless. Secondly, all fluids given to the patient and all fluids lost by the patient must be accurately charted: the information thus provided, together with an assessment of the patient's insensible loss, will always enable a reasonable estimate to be made of the patient's state of fluid balance. No single step in the care of the patient is more important than the accurate prescribing and administration of the intake, and the careful measurement and recording of the output. Many of the complications which occur after surgical operations could be avoided by this simple step, which also provides the essential information required in the control of unavoidable complications. I must apologize for ending this lecture by stressing such a mundane point as the scrupulous keeping of fluid balance charts, but it is perhaps as well in that it reminds us that despite all the apparent complexities of the subject we are in fact only dealing with comparatively simple volume problems.

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QUESTION AND ANSWER*

BY

A. H. GALLEY

QUESTION

Discuss the causation and prevention of explosions which occur during surgical operations under anaesthesia.

ANSWER

Three factors are necessary in order that an explosion may occur—an ignitable gas or vapour, a source of ignition, and the presence of oxygen to support combustion.

Ignitable vapours and gases which may be present during operations under anaesthesia are as follows:

(*a*) Inflammable anaesthetic agents, such as the ethers, cyclopropane, ethylene (not used in the United Kingdom), and ethyl chloride.

(*b*) Gastric eructations from patients with obstructions to the outlet of the stomach. The gases which have been found in such eructations are—hydrogen, methane, other hydrocarbons and sulphuretted hydrogen. Methane is thought by some to be spontaneously ignitable under certain conditions.

(*c*) Rectal flatus. The gases derived from rectal flatus usually contain large quantities of nitrogen from swallowed air, the oxygen having been absorbed during passage through the bowel. Under certain dietetic conditions, however, hydrogen, methane and sulphuretted hydrogen are generated from fermentations of the bowel contents.

(*d*) Gases produced during surgical diathermy. Hydrogen and certain hydrocarbons such as methane and ethylene are formed during the decomposition of protein tissues by the diathermy knife. It is these gases which cause most of the spluttering during surgery by diathermy, as they explode almost as soon as they are formed owing to arcing between the knife and the bodv tissues. During diathermy of the inside of he urinary bladder, however, these gases form a bubble which normally floats up out of harm's way. From time to time one hears of slight explosions within the bladder due to ignition of this bubble by the diathermy; the oxygen necessary for combustion coming from the air bubble always introduced during cystoscopy.

(*e*) Leak from coal-gas mains.

Sources of Ignition.

(*a*) *Open gas or oil heaters.* These are still used in some parts of the United Kingdom to heat sterilizers and are extensively used in the tropics.

(*b*) Static electrical discharges. These may arise from friction between various components of the anaesthetic machine; friction between towels and trolleys; friction between blankets and rubber mattresses on theatre trolleys and theatre

* This answer gives an exemplary layout for an answer, but no attempt was made to maintain examination conditions during its writing.

tables; friction between certain types of waterproof aprons and clothing; and friction between various types of plastic underclothing. Plastic mackintoshes and nylon underclothing are the frequent cause of static discharges. Even walking on non-conducting rubber or crêpe-soled shoes will charge up a person sufficiently to cause a spark should he touch an earthed object such as a water tap.

(*c*) High-frequency spark. These derive from faulty X-ray apparatus for diathermy machines.

(*d*) Faulty electrical switches, and switches which are not spark-proof. Certain types of electrical motor (e.g. those of suction machines) may also cause low-frequency sparks.

(*e*) Matches, cigarette lighters, lighted cigarettes, and similar causes which are due to gross negligence or indifference to the dangers involved.

(*f*) Accidental fires. Alcohol or iodine in alcohol is often used to cleanse a wound prior to operation. This may soak into the surgical towels or drapes, and fire results if a diathermy spark involves a moist margin of one of the towels. In operations such as the anastomosis of the ileum to the large bowel it may be thought advisable to isolate a colostomy wound by means of a dressing which is stuck to the surrounding skin by collodion solution. This solution contains ether and, if not thoroughly dry before the operation commences, a diathermy spark may again cause a fire.

(*g*) If the outlet valves (" regulators " or " reducing-valves ") of oxygen cylinders are lubricated with grease the friction caused by the oxygen passing over the lubricant may produce sufficient heat to ignite the substance used and produce a flame capable of starting an explosion.

Sources of Oxygen.

Oxygen can be obtained from the air in the operating theatre or from the oxygen cylinder used on the anaesthetic apparatus. If a fire is started there may be sufficient heat to break down nitrous oxide into nitrogen and oxygen, which latter again may be available to assist in an explosion. Oxygen swallowed during the induction of anaesthesia will be passed on to the lower bowel to render ignitable bowel gases explosive. During apnoea from muscle relaxants, inflation of the lungs with oxygen may inadvertently lead to oxygen entering the stomach; in cases of pyloric stenosis this will render the gastric gases inflammable and liable to be exploded by a static electrical spark if eructated. The presence of pure oxygen renders inflammable gases much more explosive than the presence of air.

PREVENTION OF FIRES AND EXPLOSIONS

(*a*) Reduce the use of ignitable anaesthetic agents to a minimum.

(*b*) See that ignitable substances, (anaesthetics, spirit, iodine in spirit, etc.) are not stored near a naked flame in a corner of an operating theatre, sterilizing room or " kitchen ".

(*c*) Prevent coal-gas pipes from travelling through operating theatres, and check on leaks if they do.

(*d*) Keep spirit and collodion, etc., well away from surgical wounds if diathermy is being used. Allow to dry off (from the drape as well as the skin) before using diathermy.

(*e*) Prevent sparks.

(1) Use non-sparking electric light switches and non-sparking diathermy foot switches.

(2) Use electric motors of the induction type instead of those employing copper commutators.

(3) A diathermy knife should be used correctly, i.e. the skin or haemostat should be touched with the knife before depressing the diathermy foot switch. This prevents arcing which would occur if the foot switch were depressed before the electrode touched the skin or haemostat.

(4) Diathermy should not be employed if explosive anaesthetics are in use and vice versa.

(5) Accumulation of static electrical charges should be prevented where possible, and arrangements made for their rapid discharge to earth so that high potentials (which would cause sparking) are never developed.

(6) When using diathermy in the mouth (where diathermy-decomposition gases may accumulate) or in the rectum (where ignitable flatus may be passed) a flow of nitrogen into the cavity will reduce the risk of explosion — partly because it is an inert gas and lowers the percentage of inflammable gases and partly by sweeping those gases from the cavities concerned.

Control of Static Charges.

Static electrical charges are caused by friction between electrically non-hydrogen conducting substances and materials, particularly rubber, silk, wool, and certain plastics. Plastics used in the theatre which come under this heading are nylon, polythene and perspex. The use of these substances should be eliminated. Cotton, due to its hygroscopic character, is fairly safe, as when partly moist it is sufficient of an electrical conductor to discourage static accumulations. To be more precise, therefore, one should avoid the use of plastic clothing or underclothing; avoid the use of rubber or plastic sheets and aprons; cover woollen blankets with cotton bags and use cotton dresses or operating suits. Nylon stockings are not an explosive risk as the skin protrudes through the pores of the stocking and a microscopically thin film of moisture renders them electrically conductive.

Drainage of Static Electrical Charges to Earth.

(*a*) All operating theatre apparatus, including trolleys and suction apparatus should be earthed by supplying them with electrically conducting castors.

(*b*) All the rubber parts of the anaesthetic equipment should be made of electrically conducting (" anti-static ") rubber, and castors of similar material used. In this respect it is important that *all* the rubber equipment should be so altered and not parts of it. For instance, it has been difficult to obtain face masks which were electrically conducting; if the rest of the rubber is made of this material, earth potential is brought up to within an inch or two of the patient's face which makes the likelihood of static discharge in the region of the exhaled gases more probable. The use of anti-static rubber in

the mask would of course ensure that such charges were conducted to earth. Chains suspended from trolleys are poor conductors owing to dirt and tarnish accumulating between the chain links. After a week's use they are probably useless for earthing anaesthetic and other theatre equipment.

(*c*) All personnel using the operating theatres should wear boots or shoes the soles of which are made of conducting rubber composition. In this respect it should be noted that the rubber should not be too conducting or a person wearing such shoes might accidentally come into contact with a faulty electrical switch and be electrocuted. For similar reasons the rubber Sorbo mattresses on operating trolleys and tables should have a fairly high resistance, i.e. $\frac{1}{4}$ to 1 megohm, so that current from a faulty diathermy machine should not pass through the patient to earth.

(*d*) The atmosphere in operating theatres can be made conducting, or partially conducting, by two methods: either by producing a high degree of humidity, or by ionizing the air, particularly that around the anaesthetic machine, by the use of a hair-drier in which the air passes over radio-active thallium. The former method is the cheaper, but degrees of humidity which render static discharge impossible, i.e. 70 per cent or over, are very oppressive to work in. However, 50 per cent humidity in the atmosphere is not too unpleasant and greatly reduces the risk of static discharge.

(*e*) All the above methods are useless if the flooring of the theatre does not conduct electricity to earth. Floors of oilcloth or waxed tiles are poor conductors; terrazzo floors are fairly good conductors if kept wet by moistening once or twice a day with saline solution, or a solution of calcium chloride; the latter, however, is very slippery and may be the cause of accidents. If wetting substances such as 'Tepol' are added to the saline, mopping once a day may be sufficient. The texture of terrazzo flooring is sponge-like and it holds the solution for a considerable time. Care should be taken not to earth the brass strips which are sometimes introduced in terrazzo flooring at regular intervals to prevent cracks from spreading. Should the metal wheel of an operating table be over one of these strips, and should some part of the patient's skin be touching some metal protuberance of the table, a faulty diathermy apparatus which is badly earthed may cause the electrocution of the patient. This would only occur if these metal strips were actually connected electrically with the girders of the building; this, fortunately, is rarely done.

GENERAL REMARKS

With regard to explosions, the magnitude of the problem is difficult to estimate. The Ministry of Health say that explosions are reported to them about once a month; the number of anaesthetics given per month, however, is difficult to ascertain.

One should remember the reciprocal danger, that pharmacologically dangerous anaesthetics may be given in order to avoid the use of physically dangerous (i.e. explosive) anaesthetics which are much safer in other respects; thus introducing a greater hazard to the patient than that of being blown up. An example of this would be the use of intravenous anaesthesia to a

small child for bronchoscopy when ether (which might explode if the lamp of the bronchoscope was made too hot) is safer to use from the therapeutic point of view. It may even be that deaths during anaesthesia from these causes are more numerous than those due to explosions.

Explosions of bowel gases are a real danger. Rectal flatus has been exploded during spinal anaesthesia for diathermy of a rectal polyp causing multiple tears in the wall of the colon which necessitated surgical repair.

If ignitable gases and vapours could be excluded from anaesthesia most of the danger would disappear. In the United States of America experiments are progressing in the use of flourinated ethers and cyclopropanes; these are very difficult to ignite, and one or two of the substances produced seem to be safe anaesthetics. In the United Kingdom experiments are progressing in the use of an inert gas—argon, which rather unexpectedly has proved to have anaesthetic properties. Reports to date, however, regarding its use are disappointing.

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